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# ROENTGENOLOGIC CONSIDERATIONS OF LYMPHOBLASTOMA

## I. ROENTGEN PULMONARY PATHOLOGY OF THE HODGKIN'S TYPE*

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AN IMPRESSION that the primary diseases of the lymphohemopoietic system, other than anemia, had increased in frequency during recent years led us to critically survey the records of the University Hospital for the period from July 1, 1925, to February 1, 1935. The distribution of 681 cases classified as to final diagnosis is shown in Table 1.

The present paper is concerned with the intrathoracic pathology of one-third of these, or 214 cases of Hodgkin's or sarcomatous Hodgkin's type of lymphoblastoma. In this group there has been a slight increase in number per year, but no relative increase when compared with the number of patients registered.

The clinical records of these patients have been studied as to age of patient, sex, race, initial and associated symptoms, duration of disease before admission, previous treatment, physical findings on admission, blood changes, biopsy, type of treatment, clinical, blood and roentgenographic evidence of response to treatment, length of time observed, total duration of disease, and necropsy findings. The roentgenograms of the entire series have been reviewed, save in those patients (seen only in 1925) whose films have since been destroyed. For this detailed survey, mechani-

TABLE I

Number of new patients registered July 1, 1925, to February 1, 1935—232,746

| | |
|---|---|
| Myeloblastoma | 2 |
| Chronic myelogenous leukemia | 140 |
| Monocytic leukemia | 3 |
| Aleukemic leukemia | 25 |
| Acute leukemia, blast leukemia, atypical leukemia | 74 |
| Chronic lymphatic leukemia | 21 |
| Plasmacytoma | 2 |
| Reticulocytoblastoma | 5 |
| Follicular lymphoblastoma (Rosenthal) | 1 |
| Mycosis fungoides | 11 |
| Leukemia cutis, lymphoblastoma cutis | 26 |
| Lymphoblastoma | 79 |
| Lymphosarcoma | 78 |
| Hodgkin's disease | 172 |
| Hodgkin's disease with leukemia cutis | 12 |
| Hodgkin's disease with acute leukemia | 1 |
| Sarcomatous Hodgkin's disease | 29 |
| Total | 681 |

* From the Department of Roentgenology, University of Michigan. Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

TABLE II

Legend: Col. IX Y-Positive biopsy elsewhere
Col. XI * Surgical excision of tumor.
Col. VII X = Roentgen irradiation; S = Surgical treatment; M = Medical treatment (transfusion, arsenic, or other)
Col. V * Consultation case only

| I Series Number | II Registration No. | III Age | IV Sex | V Chief Initial Symptom | VI Duration (months) | VII Previous Treatment | VIII Chief Physical Sign (on admission) |
|---|---|---|---|---|---|---|---|
| | | | NO CHEST EXAMINATION | | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 1 | 259261 | 69 | F | Adenopathy | 2 | None | Enl. spleen |
| 2 | 150242 | 21 | F | Adenopathy | 12 | None | Cerv. tumor |
| 3 | 287065 | 23 | M | *No record | | None | Gen. aden. |
| 4 | 277718 | 24 | M | *No record | | | |
| 5 | 311039 | 31 | F | *No record | | | |
| 6 | 281846 | 59 | M | *No record | | | |
| 7 | 300432 | 47 | F | Adenopathy | 4 | None | Gen. aden. |
| 8 | 273818 | 51 | M | G.-Intest. | 7 | X+Surg. | Abd. tumor |
| 9 | 169150 | 31 | M | *No record | 5 | None | Gen. aden. |
| 10 | 260724 | 47 | F | Cutaneous | 12 | None | Ing. tumor |
| 11 | 189791 | 53 | M | Adenopathy | 6 | None | Cutaneous |
| 12 | 240880 | 23 | M | Fever | 16 | None | Gen. aden. |
| 13 | 269797 | 44 | M | Cutaneous | 12 | X+M&S | Cutaneous |
| 14 | 238601 | 41 | F | Adenopathy | 12 | Loc. X | Axil. tumor |
| 15 | 237847 | 29 | M | Malaise | 8 | X+M&S | Gen. aden. |
| SARCOMATOUS HODGKIN'S DISEASE | | | | | | | |
| 16 | 302111 | 44 | M | Malaise | 7 | Loc. X | Edema |
| | | | NORMAL CHEST ROENTGENOGRAMS | | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 17 | 233223 | 48 | M | Malaise | 4 | None | Enl. spleen |
| 18 | 184612 | 41 | M | Pain | 6 | None | Gen. aden. |
| 19 | 249916 | 5 | M | Adenopathy | 3 | None | Gen. aden. |
| 20 | 340877 | 16 | M | Malaise | 12 | Med. | Cutaneous |
| 21 | 276493 | 63 | F | Adenopathy | 6 | None | Cerv. tumor |
| 22 | 164433 | 43 | M | Adenopathy | 24 | Surg. | Enl. spleen |
| 23 | 190484 | 29 | M | Adenopathy | 12 | Loc. X | Gen. aden. |
| 24 | 129952 | 33 | M | Adenopathy | 36 | Gen. X | Abd. tumor |
| 25 | 252752 | 10 | M | Adenopathy | 24 | None | Cerv. tumor |
| 26 | 242959 | 6 | M | Adenopathy | 24 | None | Cerv. tumor |
| 27 | 210767 | 11 | M | Adenopathy | 8 | None | Abd. tumor |
| 28 | 171779 | 7 | M | Adenopathy | ? | None | Gen. aden. |
| 29 | 168889 | 63 | M | G.-Intest | 3 | None | Gen. aden. |
| 30 | 326271 | 37 | M | Cutaneous | 118 | Loc. X | Cutaneous |
| 31 | 156686 | 29 | M | Adenopathy | 2 | None | Gen. aden. |
| 32 | 189842 | 26 | M | Malaise | 4 | Surg. | Axil. tumor |
| 33 | 211460 | 48 | F | Malaise | 3 | None | Gen. aden. |
| 34 | 143135 | 42 | M | Adenopathy | 6 | None | Enl. spleen |
| 35 | 192912 | 56 | M | Adenopathy | 5 | None | Gen. aden. |
| 36 | 155282 | 63 | M | Adenopathy | 3 | None | Gen. aden. |
| 37 | 289267 | 11 | M | Adenopathy | 4 | None | Gen. aden. |
| 38 | 329253 | 11 | M | G.-Intest. | 6 | None | Gen. aden. |
| 39 | 120424 | 15 | M | Adenopathy | 6 | None | Gen. aden. |
| 40 | 300024 | 22 | M | Adenopathy | 7 | None | Gen. aden. |
| 41 | 190762 | 68 | M | Adenopathy | 6 | None | Gen. aden. |
| 42 | 259653 | 33 | F | Pain | 12 | None | Aden.-Abd. tumor |
| 43 | 303233 | 55 | M | Gen.-urinary | 12 | None | Cerv. tumor |
| 44 | 345752 | 60 | M | Cutaneous | 12 | Med. | Cutaneous |
| 45 | 277721 | 69 | M | Malaise | 12 | Loc. X | Enl. spleen |
| 46 | 148155 | 54 | M | Adenopathy | 2 | None | Cerv. tumor |
| 47 | 340457 | 39 | M | Adenopathy | 7 | None | Gen. aden. |
| 48 | 153024 | 36 | M | Adenopathy | 12 | None | Edema |
| 49 | 208857 | 23 | M | Adenopathy | 12 | None | Gen. aden. |
| 50 | 291544 | 28 | M | Adenopathy | 3 | None | Cerv. tumor |

TABLE II

Legend: Col. IX Y-Positive biopsy elsewhere
Col. XI * Surgical excision of tumor.
Col. VII X = Roentgen irradiation; S = Surgical treatment; M = Medical treatment (transfusion, arsenic, or other)
Col. V * Consultation case only.

| IX Biopsy | X Year Admitted | XI Initial X-ray Treatment | XII Subsequent X-ray Treatment | XIII Duration Observation (months) | XIV Condition on Last Report | XV Autopsy | XVI Total Duration of Disease on Last Report (months) |
|---|---|---|---|---|---|---|---|
| **NO CHEST EXAMINATION** | | | | | | | |
| Pos. | 1931 | Local | Local | 10 | Dead | None | 16 |
| Pos. | 1926 | *None | None | ∞ | Good | | 36 |
| None | 1932 | None | None | ∞ | No report | | |
| | 1931 | None | | ∞ | No report | | |
| | 1933 | None | | ∞ | No report | | |
| | 1932 | None | | ∞ | No report | | |
| None | 1932 | None | | ∞ | No report | | 4 |
| Y | 1931 | None | | ∞ | Unimproved | | 10 |
| Pos. | 1927 | Local | None | 5 | Improved | | 10 |
| None | 1931 | None | None | ∞ | No record | | 12 |
| Pos. | 1928 | Local | Local | 9 | Unimproved | | 15 |
| None | 1930 | None | | ∞ | No report | | 16 |
| Pos. | 1931 | None | Systemic | 4 | Improved | | 20 |
| None | 1930 | None | | ∞ | Improved | | 25 |
| Pos. | 1930 | None | | ∞ | Worse | | 44 |
| None | 1932 | None | | ∞ | Dead | None | 8 |
| **NORMAL CHEST ROENTGENOGRAMS** | | | | | | | |
| Pos. | 1930 | Spleen | None | 1 | Dead | None | 5 |
| Pos. | 1927 | Local | None | 1 | Dead | Pos. | 7 |
| Y | 1930 | Local | None | ∞ | Dead | None | 8 |
| Pos. | 1934 | Local | None | ∞ | Dead | None | 12 |
| Pos. | 1931 | Local | None | 6 | Dead | None | 12 |
| Y | 1929 | None | None | ∞ | Dead | None | 24 |
| Pos. | 1928 | Local | Local | 13 | Dead | Pos. | 27 |
| Y | 1933 | None | None | ∞ | Dead | None | 36 |
| Pos. | 1930 | Local | Local | 19 | Dead | Pos. | 43 |
| Pos. | 1930 | Local | Local | 22 | Dead | None | 46 |
| Pos. | 1929 | Local | Local | 38 | Dead | None | 47 |
| Pos. | 1927 | Local | Local | 30 | Dead | None | 48 |
| Pos. | 1927 | Local | Local | 52 | Dead | Pos. | 55 |
| Pos. | 1933 | Local | Systemic | 59 | Dead | None | 182 |
| Y | 1926 | Local | None | 1 | No report | | 3 |
| Y | 1930 | None | None | ∞ | No report | | 4 |
| Pos. | 1929 | None | None | 2 | No report | | 5 |
| None | 1926 | Local | None | 1 | Improved | | 7 |
| Pos. | 1928 | *Local | None | 2 | Improved | | 7 |
| Pos. | 1926 | Local | Local | 5 | Improved | | 8 |
| Pos. | 1932 | Systemic | None | 5 | Clinically well | | 9 |
| Pos. | 1935 | Systemic | None | 3 | Improved | | 9 |
| None | 1925 | Local | None | 3 | Improved | | 9 |
| Pos. | 1932 | Systemic | Systemic | 3 | Improved | | 10 |
| None | 1928 | Local | Local | 5 | Improved | | 11 |
| Pos. | 1931 | Local | None | ∞ | Unchanged | | 12 |
| Pos. | 1932 | None | None | ∞ | No report | | 12 |
| None | 1934 | None | None | ∞ | No report | | 12 |
| None | 1931 | None | None | ∞ | No report | | 12 |
| Pos. | 1926 | Local | None | ∞ | No report | | 12 |
| Pos. | 1934 | None | None | ∞ | Worse | | 13 |
| Pos. | 1926 | Local | None | 1 | No report | | 13 |
| Pos. | 1929 | Local | None | 2 | Improved | | 14 |
| None | 1932 | Local | None | 13 | Improved | | 16 |

TABLE II (*Continued*)

| I Series Number | II Registration No. | III Age | IV Sex | V Chief Initial Symptom | VI Duration (months) | VII Previous Treatment | VIII Chief Physical Sign (on admission) |
|---|---|---|---|---|---|---|---|
| 51 | 331730 | 16 | M | Adenopathy | 12 | None | Gen. aden. |
| 52 | 355659 | 64 | M | Adenopathy | 12 | None | Axil. tumor |
| 53 | 217249 | 31 | M | Pain | 12 | None | Gen. aden. |
| 54 | 293173 | 13 | M | Adenopathy | 12 | Loc. X | Gen. aden. |
| 55 | 169969 | 57 | M | Adenopathy | 18 | Radium | Axil. tumor |
| 56 | 286711 | 13 | F | Malaise | 1 | None | Enl. spleen |
| 57 | 316446 | 52 | F | Adenopathy | 10 | None | Cerv. tumor |
| 58 | 120883 | 12 | M | Adenopathy | 6 | None | Cerv. tumor |
| 59 | 137243 | 37 | M | Adenopathy | 24 | Loc. X | Cerv. tumor |
| 60 | 165227 | 48 | M | Adenopathy | 24 | Gen. X | Edema |
| 61 | 245124 | 17 | M | C.-Respirat. | 24 | None | Cerv. tumor |
| 62 | 232594 | 28 | M | Adenopathy | 24 | None | Axil. tumor |
| 63 | 232620 | 22 | F | Adenopathy | 16 | None | Axil. tumor |
| 64 | 261771 | 26 | M | Adenopathy | 18 | None | Enl. spleen |
| 65 | 214184 | 39 | M | Adenopathy | 12 | None | Abd. tumor |
| 66 | 263816 | 42 | F | Adenopathy | 24 | None | Gen. aden. |
| 67 | 332404 | 13 | M | Adenopathy | 12 | Loc. X | Gen. aden. |
| 68 | 151568 | 22 | F | Adenopathy | 24 | None | Cerv. tumor |
| 69 | 122228 | 4 | M | Adenopathy | 6 | None | Cerv. tumor |
| 70 | 266521 | 35 | M | Fever | 36 | Loc. X | Gen. aden. |
| 71 | 328051 | 59 | M | Pain | 24 | None | Gen. aden. |
| 72 | 122593 | 7 | M | Adenopathy | 12 | None | Gen. aden. |
| 73 | 351349 | 13 | M | C.-Respirat. | 36 | None | Axil. tumor |
| 74 | 290563 | 12 | M | Adenopathy | 1 | None | Cerv. tumor |
| 75 | 280010 | 28 | M | G.-Intest. | 12 | None | Gen. aden. |
| 76 | 213310 | 61 | F | Malaise | 24 | None | Cerv. tumor |
| 77 | 124528 | 71 | F | Malaise | 36 | None | Enl. spleen |
| 78 | 282681 | 47 | M | Gen.-urinary | 60 | None | Enl. spleen |
| 79 | 136342 | 33 | F | Adenopathy | 66 | Loc. X | Gen. aden. |
| 80 | 150023 | 44 | M | Adenopathy | 48 | None | Gen. aden. |
| 81 | 188349 | 13 | M | Adenopathy | 24 | S&X | Cutaneous |
| 82 | 132555 | 19 | F | Adenopathy | 12 | Loc. X | Gen. aden. |
| 83 | 123054 | 16 | M | Adenopathy | 60 | Surg. | Gen. aden. |
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 84 | 252062 | 1 | M | Adenopathy | 2 | None | Edema |
| 85 | 220212 | 23 | M | Pain | 12 | None | Enl. spleen |
| 86 | 258407 | 40 | M | Adenopathy | 20 | Surg. | Cutaneous |
| 87 | 232418 | 7 | F | Adenopathy | 12 | Med. | Cerv. tumor |
| 88 | 272871 | 29 | M | Malaise | 8 | Med. | Ing. tumor |
| 89 | 315162 | 26 | M | Adenopathy | 8 | None | Cerv. tumor |
| 90 | 324935 | 13 | M | Adenopathy | 18 | None | Cerv. tumor |
| | | | | HILAR ADENOPATHY | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 91 | 255084 | 12 | M | Adenopathy | 6 | None | Gen. aden. |
| 92 | 148393 | 21 | M | Malaise | 1 | None | Enl. spleen |
| 93 | 280383 | 66 | M | Adenopathy | 84 | X-ray | Gen. aden. |
| 94 | 192990 | 67 | F | Adenopathy | 1 | None | Cutaneous |
| 95 | 241233 | 27 | M | Malaise | 6 | Loc. X | Gen. aden. |
| 96 | 356674 | 59 | M | Adenopathy | 1 | Surg. | Edema |
| 97 | 340310 | 45 | M | Adenopathy | 11 | Loc. X | Cerv. aden. |
| 98 | 348860 | 15 | M | Adenopathy | 5 | None | Pulmonary |
| 99 | 147941 | 38 | F | C.-Respirat. | 12 | None | Cutaneous |
| 100 | 322162 | 12 | M | Adenopathy | 18 | Loc. X | Gen. aden. |
| 101 | 337716 | 66 | F | Adenopathy | 18 | Loc. X | Edema |
| 102 | 196520 | 33 | M | Pain | 12 | Surg. | Enl. spleen |
| 103 | 291291 | 33 | M | Adenopathy | 18 | Med. | Cutaneous |
| 104 | 120857 | 31 | F | Adenopathy | 36 | None | Enl. spleen |
| 105 | 234986 | 45 | F | Adenopathy | 42 | Med. | Gen. aden. |
| 106 | 207914 | 50 | F | Malaise | 6 | None | Axil. tumor |
| 107 | 349645 | 51 | M | Adenopathy | 48 | Loc. X | Axil. tumor |
| 108 | 324793 | 19 | F | Adenopathy | 36 | None | Gen. aden. |
| 109 | 280080 | 19 | M | Pain | 24 | None | Gen. aden. |

Table II (*Continued*)

| IX Biopsy | X Year Admitted | XI Initial X-ray Treatment | XII Subsequent X-ray Treatment | XIII Duration Observation (months) | XIV Condition on Last Report | XV Autopsy | XVI Total Duration of Disease on Last Report (months) |
|---|---|---|---|---|---|---|---|
| Pos. | 1934 | Systemic | None | 4 | Worse | | 16 |
| Pos. | 1935 | Systemic | None | 5 | Improved | | 17 |
| None | 1929 | None | None | 6 | Unimproved | | 18 |
| Pos. | 1932 | None | None | ∞ | Improved | | 18 |
| Y | 1927 | Systemic | None | 1 | Improved | | 19 |
| None | 1932 | None | None | 19 | Unimproved | | 20 |
| Y | 1933 | Systemic | None | 10 | Clinically well | | 21 |
| Pos. | 1925 | Local | Local | 16 | Improved | | 22 |
| Pos. | 1926 | Local | None | ∞ | No report | | 24 |
| Pos. | 1927 | None | None | ∞ | No report | | 24 |
| Pos. | 1930 | Local | None | 2 | Improved | | 26 |
| Pos. | 1930 | Local | None | 3 | Improved | | 27 |
| None | 1930 | Local | None | 1 | Improved | | 27 |
| Pos. | 1931 | Local | None | 1 | Improved | | 27 |
| Pos. | 1929 | Local | None | 3 | Improved | | 27 |
| Pos. | 1931 | Local | None | 3 | Improved | | 27 |
| Pos. | 1934 | Local | Systemic | 16 | Clinically well | | 28 |
| None | 1926 | Ra Cl | Local | 4 | Improved | | 28 |
| Pos. | 1925 | Local | Local | 14 | Improved | | 32 |
| Pos. | 1931 | None | None | ∞ | No report | | 36 |
| Y | 1934 | Local | Local | 6 | Clinically well | | 36 |
| Pos. | 1925 | Local | Local | 25 | Worse | | 37 |
| Pos. | 1934 | Systemic | Systemic | 6 | Improved | | 42 |
| Pos. | 1933 | None | Systemic | 30 | Unimproved | | 43 |
| Pos. | 1931 | None | Local | 37 | Unimproved | | 48 |
| None | 1929 | None | Local | 12 | Improved | | 50 |
| None | 1925 | Ra Cl | Local | 29 | Worse | | 65 |
| None | 1932 | None | None | 9 | Unimproved | | 69 |
| Pos. | 1925 | Local | Local | 3 | Improved | | 69 |
| Pos. | 1926 | *None | None | 30 | Improved | | 82 |
| Pos. | 1928 | Local | Local | 90 | Clinically well | | 114 |
| Pos. | 1924 | Local | None | 104 | Clinically well | | 130 |
| Pos. | 1925 | Local+ Ra Cl | Systemic | 105 | Clinically well | | 165 |
| Pos. | 1930 | None | None | 3 | Dead | Pos. | 5 |
| Pos. | 1929 | Local | None | 7 | Dead | None | 19 |
| Pos. | 1931 | *None | None | ∞ | Dead | None | 21 |
| Y-Pos. | 1930 | Local | Local | 15 | Dead | None | 27 |
| Pos. | 1931 | Local | None | 1 | Improved | | 9 |
| Pos. | 1933 | Systemic | None | 18 | Improved | | 28 |
| Pos. | 1933 | Systemic | Systemic | 25 | Clinically well | | 43 |
| | | | HILAR ADENOPATHY | | | | |
| Pos. | 1930 | Local | None | 1 | Dead | None | 8 |
| Pos. | 1934 | Systemic | Systemic | 10 | Dead | Pos. | 11 |
| Pos. | 1931 | Local | Local | 4 | Dead | None | 92 |
| Pos. | 1928 | Local | None | 1 | Improved | | 2 |
| Y | 1930 | None | None | ∞ | No report | | 6 |
| Y | 1935 | Systemic | None | ∞ | No report | | 1 |
| Y | 1934 | Systemic | None | 1 | Clinically well | | 15 |
| Pos. | 1934 | Systemic | Systemic | 8 | Improved | | 13 |
| Pos. | 1926 | Local | None | 2 | Improved | | 14 |
| Pos. | 1933 | None | None | ∞ | No report | | 18 |
| Pos. | 1934 | Local | None | ∞ | No report | | 18 |
| Pos. | 1928 | Local | Local | 8 | Worse | | 20 |
| Pos. | 1932 | Local | None | 4 | Worse | | 22 |
| None | 1925 | None | | ∞ | No report | | 36 |
| None | 1930 | Local | Local | 3 | Unimproved | | 45 |
| None | 1931 | Local | None | 40 | Clinically well | | 47 |
| Y | 1934 | Systemic | None | 4 | Improved | | 52 |
| Y | 1933 | Systemic | Local | 21 | Clinically well | | 57 |
| Pos. | 1931 | None | None | 38 | Unimproved | | 62 |

TABLE II (*Continued*)

| I Series Number | II Registration No. | III Age | IV Sex | V Chief Initial Symptom | VI Duration (months) | VII Previous Treatment | VIII Chief Physical Sign (on admission) |
|---|---|---|---|---|---|---|---|
| 110 | 170626 | 24 | M | G.-Intest. | 60 | None | Cutaneous |
| 111 | 255602 | 8 | M | Adenopathy | 12 | None | Gen. aden. |
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 112 | 275877 | 10 | M | Adenopathy | 48 | X, M&S | Abd. tumor |
| | | | | MEDIASTINAL TUMOR | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 113 | 313966 | 20 | M | Adenopathy | 3 | None | Gen. aden. |
| 114 | 160735 | 38 | M | Adenopathy | 9 | Loc. X | Gen. aden. |
| 115 | 189346 | 5 | M | Pain | 12 | None | Abd. tumor |
| 116 | 300941 | 20 | M | Adenopathy | 12 | Loc. X | Gen. aden. |
| 117 | 136064 | 35 | F | Malaise | 18 | Loc. X | Abd. tumor |
| 118 | 255128 | 15 | F | Adenopathy | 1 | None | Cutaneous |
| 119 | 225551 | 27 | F | Adenopathy | 6 | None | Gen. aden. |
| 120 | 163305 | 19 | M | Malaise | 14 | Loc. X | Gen. aden. |
| 121 | 123227 | 29 | M | Adenopathy | 2 | None | Gen. aden. |
| 122 | 202871 | 21 | F | Adenopathy | 30 | Gen. X | Gen. aden. |
| 123 | 274150 | 21 | F | Malaise | 24 | None | Cerv. tumor |
| 124 | 304074 | 26 | M | Adenopathy | 48 | Surg. | Cerv. tumor |
| 125 | 203064 | 13 | M | Adenopathy | 96 | None | Enl. spleen |
| 126 | 120510 | 34 | F | Adenopathy | 1 | None | Cerv. tumor |
| 127 | 287103 | 15 | M | Adenopathy | 4 | None | Gen. aden. |
| 128 | 258827 | 30 | F | Adenopathy | 5 | None | Abd. tumor |
| 129 | 130324 | 41 | M | Pain | 1 | None | Ing. tumor |
| 130 | 230438 | 59 | M | Adenopathy | 6 | None | Edema |
| 131 | 356637 | 47 | M | Adenopathy | 4 | None | Edema |
| 132 | 239537 | 20 | M | G.-Intest. | 9 | None | Cerv. tumor |
| 133 | 141291 | 51 | F | Adenopathy | 6 | None | Gen. aden. |
| 134 | 167645 | 40 | M | Adenopathy | 6 | None | Gen. aden. |
| 135 | 153816 | 22 | M | Malaise | 9 | None | Gen. aden. |
| 136 | 202949 | 16 | M | Adenopathy | 12 | None | Edema |
| 137 | 331853 | 20 | F | Adenopathy | 12 | None | Gen. aden. |
| 138 | 149801 | 25 | F | Malaise | 12 | Med. | Gen. aden. |
| 139 | 236714 | 21 | M | Malaise | 3 | None | Cerv. tumor |
| 140 | 352261 | 31 | M | Adenopathy | 10 | None | Cutaneous |
| 141 | 227386 | 41 | F | Adenopathy | 12 | Med. | Cutaneous |
| 142 | 326813 | 17 | M | Fever | 3 | None | Gen. aden. |
| 143 | 246884 | 21 | M | Malaise | 28 | Loc. X | Enl. spleen |
| 144 | 282451 | 26 | F | Adenopathy | 14 | None | Cerv. tumor |
| 145 | 335512 | 37 | F | Malaise | 24 | None | Enl. spleen |
| 146 | 321813 | 25 | M | Adenopathy | 12 | None | Gen. aden. |
| 147 | 122759 | 36 | F | Adenopathy | 24 | X, M&S | Gen. aden. |
| 148 | 253531 | 19 | M | C.-Respirat. | 3 | None | Pulmonary |
| 149 | 317450 | 30 | M | Adenopathy | 22 | Loc. X | Edema |
| 150 | 290869 | 35 | F | Cutaneous | 48 | Loc. X | Enl. spleen |
| 151 | 248623 | 18 | F | Malaise | 3 | None | Cerv. tumor |
| 152 | 166378 | 55 | M | Pain | 60 | None | Pulmonary |
| 153 | 214651 | 21 | F | Adenopathy | 48 | None | Cerv. tumor |
| 154 | 208518 | 30 | M | Malaise | 60 | None | Pulmonary |
| 155 | 335138 | 26 | F | Malaise | 96 | None | Enl. spleen |
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 156 | 121501 | 39 | M | Adenopathy | 8 | None | Edema |
| 157 | 191047 | 69 | M | Adenopathy | 2 | None | Edema |
| | | | | MEDIASTINAL TUMOR AND HILAR ADENOPATHY | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 158 | 239085 | 37 | M | Adenopathy | 6 | None | Ing. tumor |
| 159 | 217829 | 17 | F | Malaise | 24 | None | Gen. aden. |
| 160 | 326538 | 22 | M | Adenopathy | 19 | Loc. X | Ing. tumor |
| 161 | 336094 | 17 | F | Malaise | 48 | Loc. X | Enl. spleen |

Table II (*Continued*)

| IX Biopsy | X Year Admitted | XI Initial X-ray Treatment | XII Subsequent X-ray Treatment | XIII Duration Observation (months) | XIV Condition on Last Report | XV Autopsy | XV Total Duration of Disease on Last Report (months) |
|---|---|---|---|---|---|---|---|
| None | 1927 | None | Local | 3 | Improved | | 63 |
| Pos. | 1930 | Local | Systemic | 55 | Clinically well | | 67 |
| Pos. | 1931 | Local | Systemic | 24 | Dead | Pos. | 72 |
| | | | MEDIASTINAL TUMOR | | | | |
| None | 1933 | Systemic | Systemic | 5 | Dead | Pos. | 8 |
| None | 1927 | Local | None | ∞ | Dead | Pos. | 10 |
| None | 1928 | None | None | ∞ | Dead | Pos. | 12 |
| Pos. | 1932 | Systemic | Systemic | 5 | Dead | Pos. | 17 |
| Pos. | 1926 | Local | None | 2 | Dead | Pos. | 20 |
| Pos. | 1930 | Local | Local | 20 | Dead | None | 21 |
| Pos. | 1929 | Local | Local | 17 | Dead | Pos. | 23 |
| Pos. | 1927 | Local | Skeletal | 11 | Dead | None | 26 |
| Pos. | 1925 | Local | Ra Cl | 34 | Dead | None | 36 |
| Pos. | 1928 | Local | Local | 13 | Dead | Pos. | 43 |
| None | 1931 | Local | Local | 12 | Dead | None | 50 |
| Pos. | 1932 | Systemic | Systemic | 11 | Dead | None | 59 |
| None | 1928 | Local | None | ∞ | Dead | None | 96 |
| None | 1925 | Local | None | 1 | Improved | | 3 |
| Pos. | 1932 | Local | None | 1 | Improved | | 5 |
| Pos. | 1931 | Local | None | 1 | Improved | | 6 |
| None | 1925 | Local | Local | 6 | Worse | | 6 |
| Pos. | 1929 | None | None | ∞ | No report | | 6 |
| None | 1935 | Systemic | None | 4 | Improved | | 8 |
| Pos. | 1930 | None | | ∞ | No report | | 9 |
| None | 1926 | Local | None | 3 | Improved | | 9 |
| Pos. | 1927 | Local | Local | 3 | Unimproved | | 9 |
| Pos. | 1926 | Local | None | 2 | Improved | | 11 |
| Pos. | 1928 | None | | ∞ | No report | | 12 |
| Pos. | 1934 | None | | ∞ | No report | | 12 |
| Pos. | 1926 | Local | None | 1 | No report | | 13 |
| None | 1931 | Local | None | 12 | Improved | | 15 |
| Pos. | 1935 | Systemic | Systemic | 6 | Clinically well | | 16 |
| Pos. | 1929 | Local | Local | 8 | Clinically well | | 20 |
| Y | 1933 | Systemic | None | 21 | Clinically well | | 24 |
| Pos. | 1930 | Local | None | ∞ | No report | | 28 |
| Pos. | 1932 | Systemic | Systemic | 14 | Improved | | 28 |
| None | 1934 | Systemic | None | 4 | Improved | | 28 |
| Pos. | 1933 | Systemic | Systemic | 20 | Improved | | 32 |
| Pos. | 1925 | Local | Local | 9 | Improved | | 33 |
| None | 1931 | Local | None | 9 | Clinically well | | 37 |
| Y | 1933 | Skeletal | Systemic | 21 | Improved | | 43 |
| Pos. | 1932 | Local | None | 1 | Improved | | 49 |
| Pos. | 1930 | Local | Systemic | 49 | Improved | | 52 |
| None | 1927 | Local | None | ∞ | Worse | | 62 |
| Pos. | 1929 | Local | Local | 20 | Clinically well | | 68 |
| None | 1933 | Systemic | None | 21 | Clinically well | | 81 |
| Pos. | 1934 | Systemic | None | 2 | Clinically well | | 98 |
| Pos. | 1925 | Local | None | 3 | Dead | None | 11 |
| Pos. | 1928 | Local | Local | 77 | Dead | Pos. | 9 |
| | | | MEDIASTINAL TUMOR AND HILAR ADENOPATHY | | | | |
| Pos. | 1930 | Local | Systemic | 55 | Dead | None | 60 |
| None | 1929 | None | | ∞ | No report | | 24 |
| Pos. | 1933 | Systemic | Systemic | 18 | Clnically well | | 37 |
| None | 1934 | Systemic | Systemic | 7 | Clinically well | | 55 |

TABLE II (*Continued*)

| I Series Number | II Registration No. | III Age | IV Sex | V Chief Initial Symptom | VI Duration (months) | VII Previous Treatment | VIII Chief Physical Sign (on admission) |
|---|---|---|---|---|---|---|---|
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 162 | 198966 | 33 | M | Adenopathy | 7 | None | Enl. spleen |
| 163 | 265193 | 47 | M | Malaise | 12 | Loc. X | Gen. aden. |
| 164 | 288324 | 30 | M | Adenopathy | 12 | Med. | Gen. aden. |
| 165 | 276561 | 45 | M | Pain | 6 | None | Gen. aden. |
| PARENCHYMATOUS INVOLVEMENT | | | | | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 166 | 268042 | 29 | M | Malaise | 30 | Loc. X | Enl. spleen |
| 167 | 127434 | 12 | F | Adenopathy | 24 | None | Gen. aden. |
| 168 | 261858 | 33 | F | Adenopathy | 12 | None | Enl. spleen |
| 169 | 188182 | 27 | M | Cardio-resp. | 4 | None | Pulmonary |
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 170 | 275609 | 46 | F | Cardio-resp. | 80 | X, M&S | Cutaneous |
| 171 | 303937 | 8 | M | Adenopathy | 24 | None | Axil. tumor. |
| PARENCHYMATOUS INVOLVEMENT AND HILAR ADENOPATHY | | | | | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 172 | 274772 | 8 | M | Malaise | 4 | Loc. X | Enl. spleen |
| 173 | 321451 | 28 | M | Fever | 6 | Surg. | Gen. aden. |
| 174 | 244294 | 33 | F | Adenopathy | 12 | None | Gen. aden. |
| 175 | 298241 | 29 | F | Adenopathy | 24 | None | Cutaneous |
| 176 | 332531 | 28 | F | Adenopathy | 18 | Surg. | Gen. aden. |
| 177 | 361638 | 42 | F | G.-Intest. | 36 | Med. | Abd. tumor |
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 178 | 259053 | 49 | M | Adenopathy | 3 | None | Axil. tumor |
| 179 | 299397 | 30 | M | Cardio-resp. | 18 | Loc. X | Gen. aden. |
| 180 | 226491 | 10 | M | Adenopathy | 12 | Med. | Enl. spleen |
| 181 | 345438 | 45 | M | Adenopathy | 18 | Loc. X | Cutaneous |
| PARENCHYMATOUS INVOLVEMENT AND MEDIASTINAL TUMOR | | | | | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 182 | 217655 | 37 | M | Malaise | 8 | None | Edema |
| 183 | 235759 | 13 | M | Cutaneous | 4 | None | Cutaneous |
| 184 | 134499 | 27 | F | Adenopathy | 24 | Loc. X | Edema |
| 185 | 265273 | 44 | F | Malaise | 24 | None | Edema |
| 186 | 217105 | 26 | M | Adenopathy | 8 | Loc. X | Axil. tumor |
| 187 | 332936 | 15 | M | Cardio-resp. | 2 | None | Cutaneous |
| 188 | 298548 | 27 | M | Malaise | 6 | None | Gen. aden. |
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 189 | 299111 | 46 | M | Malaise | 24 | Med. | Cutaneous |
| PARENCHYMATOUS, HILAR AND MEDIASTINAL INVOLVEMENT | | | | | | | |
| HODGKIN'S | | | | | | | |
| 190 | 311184 | 33 | M | Cardio-resp. | 12 | Med. | Enl. spleen |
| 191 | 238054 | 18 | M | Edema | 14 | Loc. X | Gen. aden. |
| 192 | 310638 | 21 | M | Loss weight | 3 | None | Edema |
| PLEURAL INVOLVEMENT WITH OR WITHOUT OTHER OF THE ABOVE | | | | | | | |
| HODGKIN'S DISEASE | | | | | | | |
| 193 | 304422 | 34 | M | Adenopathy | 4 | Loc. X | Edema |
| 194 | 201938 | 27 | M | Adenopathy | 12 | Gen. X | Enl. spleen |
| 195 | 158183 | 29 | M | Fever | 12 | None | Enl. spleen |
| 196 | 275697 | 30 | M | Cardio-resp. | 9 | None | Gen. aden. |
| 197 | 159054 | 21 | M | Adenopathy | 8 | None | Gen. aden. |
| 198 | 212748 | 19 | M | Adenopathy | 24 | Loc. X | Enl. spleen |

TABLE II (*Continued*)

| IX Biopsy | X Year Admitted | XI Initial X-ray Treatment | XII Subsequent X-ray Treatment | XIII Duration Observation (months) | XIV Condition on Last Report | XV Autopsy | XVI Total Duration of Disease on Last Report (months) |
|---|---|---|---|---|---|---|---|
| Pos. | 1928 | Local | Local | 6 | Worse | | 13 |
| Pos. | 1931 | Local | None | ∞ | Improved | | 13 |
| Pos. | 1932 | Local | Systemic | 10 | Improved | | 22 |
| Pos. | 1931 | Local | None | ∞ | Clinically well | | 37 |
| | | | PARENCHYMATOUS INVOLVEMENT | | | | |
| Pos. | 1931 | Spleen | None | 2 | Dead | Pos. | 32 |
| Pos. | 1925 | Local | Local | 78 | Dead | Pos. | 102 |
| Pos. | 1931 | None | None | ∞ | No report | | 12 |
| None | 1932 | Local | None | 6 | Clinically well | | 31 |
| Y | 1931 | None | None | 1 | Dead | Pos | 81 |
| Pos. | 1932 | Systemic | Systemic | 23 | Critical | | 47 |
| | | | PARENCHYMATOUS INVOLVEMENT AND HILAR ADENOPATHY | | | | |
| Pos. | 1931 | None | None | ∞ | Dead | None | 4 |
| Pos. | 1933 | None | None | 1 | Unimproved | | 8 |
| Y | 1930 | Local | Local | 10 | Worse | | 22 |
| Pos. | 1932 | Systemic | None | 1 | Improved | | 25 |
| Pos. | 1934 | Systemic | Systemic | 6 | Improved | | 29 |
| Pos. | 1935 | Systemic | None | 1 | No report | | 36 |
| Y | 1931 | Local | Local | 7 | Dead | None | 10 |
| Pos. | 1932 | Local | None | 1 | Dead | Pos. | 19 |
| Pos. | 1929 | Local & Spleen | Local | 24 | Dead | None | 37 |
| Pos. | 1934 | Systemic | Local | 6 | Worse | | 24 |
| | | | PARENCHYMATOUS INVOLVEMENT AND MEDIASTINAL TUMOR | | | | |
| Pos. | 1929 | None | None | 1 | Dead | Pos. | 9 |
| Pos. | 1930 | Local | None | 10 | Dead | None | 21 |
| None | 1926 | Local | None | 1 | Dead | Pos. | 25 |
| Pos. | 1931 | Local | Local | 29 | Dead | Pos. | 53 |
| Pos.-Y | 1929 | Local | None | 5 | Improved | | 13 |
| Pos. | 1934 | Systemic | Systemic | 15 | Clinically well | | 17 |
| None | 1932 | Systemic | Systemic | 30 | Clinically well | | 36 |
| Pos. | 1932 | Local | Systemic | 27 | Improved | | 51 |
| | | | PARENCHYMATOUS, HILAR AND MEDIASTINAL INVOLVEMENT | | | | |
| Pos.-Y | 1933 | Systemic | Systemic | 17 | Dead | None | 29 |
| Pos.-Y | 1930 | Local | Local | 20 | Dead | Pos. | 34 |
| None | 1933 | Systemic | Systemic | 9 | Clinically well | | 12 |
| | | | PLEURAL INVOLVEMENT WITH OR WITHOUT OTHER OF THE ABOVE | | | | |
| Pos. | 1932 | None | None | ∞ | Dead | Pos. | 4 |
| None | 1928 | None | None | 1 | Dead | None | 13 |
| Pos. | 1926 | Local | None | ∞ | Dead | Pos. | 13 |
| Pos. | 1931 | Local | Local | 5 | Dead | None | 14 |
| Pos. | 1926 | Local | Local | 15 | Dead | Pos. | 23 |
| Pos.-Y | 1929 | Local | Local | 11 | Dead | Pos. | 35 |

TABLE II (*Continued*)

| I Series Number | II Registration No. | III Age | IV Sex | V Chief Initial Symptom | VI Duration (months) | VII Previous Treatment | VIII Chief Physical Sign (on admission) |
|---|---|---|---|---|---|---|---|
| 199 | 167002 | 37 | M | G.-Intest. | 2 | None | Gen. aden. |
| 200 | 309647 | 71 | M | G.-Intest. | 7 | None | Abd. tumor |
| 201 | 320356 | 52 | F | Malaise | 6 | None | Gen. aden. |
| 202 | 149373 | 40 | F | Pain | 6 | Med. | Gen. aden. |
| 203 | 297378 | 58 | F | Cardio-resp. | 24 | None | Gen. aden. |
| 204 | 238638 | 30 | M | Adenopathy | 36 | None | Enl. spleen |
| 205 | 351494 | 53 | M | Cardio-resp. | 36 | None | Abd. tumor |
| 206 | 233957 | 24 | F | Adenopathy | 60 | X. & Surg. | Enl. spleen |
| 207 | 252202 | 25 | F | Adenopathy | 72 | Loc. X | Gen. aden. |
| SARCOMATOUS HODGKIN'S | | | | | | | |
| 208 | 221175 | 65 | M | Adenopathy | 4 | None | Axil. tumor |
| 209 | 273115 | 44 | M | Cardio-resp. | 36 | None | Enl. spleen |
| 210 | 240325 | 46 | M | G.-Intest. | 42 | Surg. | Cutaneous |
| 211 | 337979 | 40 | M | Malaise | 3 | None | Enl. spleen |
| 212 | 287977 | 73 | F | Night sweats | 2 | None | Enl. spleen |
| 213 | 351811 | 51 | M | Pain | 4 | None | Edema |
| 214 | 220596 | 35 | M | Malaise | 10 | None | Edema |

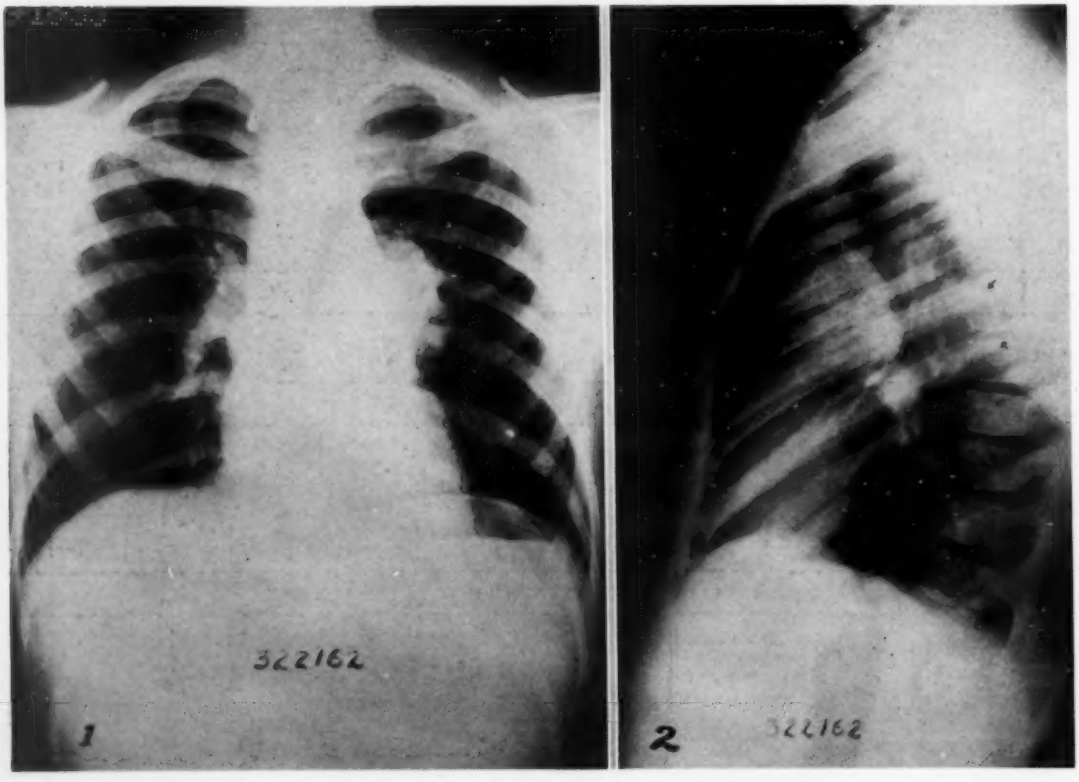



PLATE I. *Hilar.* No. 322162 (Serial 100). Male, aged twelve. Swollen neck for eighteen months, fever, weight loss, anorexia. Generalized adenopathy. Tuberculin test negative. Biopsy: Hodgkin's disease. No subsequent information.

FIG. 1. Left hilar adenopathy.

FIG. 2. Lateral: Pericarinal glands enlarged; gross size of posterior nodes.

TABLE II (*Continued*)

| IX Biopsy | X Year Admitted | XI Initial X-ray Treatment | XII Subsequent X-ray Treatment | XIII Duration Observation (months) | XIV Condition on Last Report | XV Autopsy | XVI Total Duration Disease on Last Report (months) |
|---|---|---|---|---|---|---|---|
| Pos. | 1927 | Local | None | 2 | Improved | | 4 |
| None | 1933 | Systemic | None | ∞ | No report | | 7 |
| Pos. | 1933 | Systemic | Local | 6 | Worse | | 12 |
| None | 1926 | None | None | 9 | Improved | | 15 |
| Pos. | 1932 | Systemic | Systemic | 10 | Improved | | 34 |
| Pos. | 1930 | None | None | ∞ | No report | | 36 |
| Y | 1935 | Systemic | Systemic | 8 | Improved | | 43 |
| Pos.-Y | 1930 | Local | Local | 14 | Worse | | 74 |
| Y | 1930 | Local | None | ∞ | Critical | | 78 |
| Pos. | 1929 | None | None | ∞ | Dead | None | 4 |
| Pos. | 1931 | None | None | 90 | Dead | None | 36 |
| Pos.-Y | 1930 | Local | None | 5 | Dead | None | 48 |
| Pos. | 1934 | Radium | None | ∞ | Critical | | 3 |
| Pos. | 1932 | None | None | 2 | No report | | 5 |
| Pos. | 1935 | Systemic | Systemic | 4 | Improved | | 8 |
| Pos. | 1929 | None | None | 1 | Worse | | 15 |

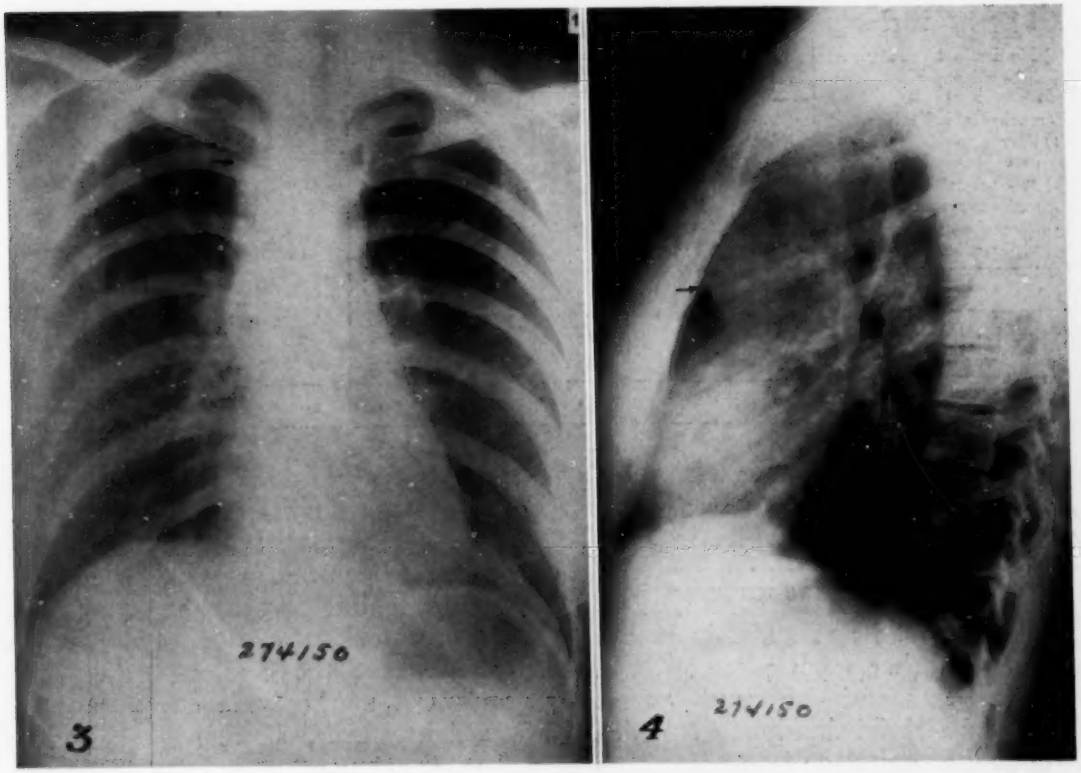



PLATE II. *Mediastinal.* No. 274150 (Serial 123). Female aged twenty-one. Weakness for two years, fatigue, weight loss, abdominal pain. Pallor, cervical adenopathy.

FIG. 3. Loss of curvilinear contour of supracardiac shadow, bilaterally—extension into thoracic inlet.

FIG. 4. Lateral: Sharply marginated soft tissue obscuration of retrosternal space. Improved under local irradiation. Death at home two years later.

cal sorting and tabulating devices have facilitated comparison of the information gleaned from the individual records.

The entire series, with some of the individual data, is listed in Table II, in order of known duration of disease, those known to be dead, and those alive on last report, grouped separately. It has been impossible to determine the final outcome of many cases because of the character of the patient population in our institution.

relatives with known lymphoblastoma, less than 10 per cent with known carcinoma or sarcoma in the two immediate generations. Contact with tuberculosis seemed to bear no relationship. Two patients in the series developed pulmonary tuberculosis in the terminal stages of their disease.

Over one-half of the series had received no treatment before admission. One-fourth had had some previous roentgen irradiation.

TABLE III

| Roentgenologic Findings in Chest | Number of Cases | Average Duration of Symptoms before Admission (Minimum) (Maximum) in Months | Hodgkin's Disease | Hodgkin's Disease with Leukemia Cutis | Hodgkin's Disease with Aleukemic Leukemia | Sarcomatous Hodgkin's Disease | Average Period Observed (Miminum) (Maximum) in Months | Average Duration of Disease or Last Report (Minimum) (Maximum) in Months | Known Deaths |
|---|---|---|---|---|---|---|---|---|---|
| Not examined | 16 | 8 (2–16) | 13 | 2 | 0 | 1 | 2 (0–10) | 13 (4–44) | 2 |
| (a) Normal lung and mediastinum | 74 | 15 (2–118) | 64 | 3 | 0 | 7 | 9.3 (0–105) | 31 (3–182) | 18 |
| (b) Tumor or adenopathy | | | | | | | | | |
| (1) Hilar adenopathy only | 22 | 23 (1–84) | 19 | 2 | 0 | 1 | 10.2 (0–55) | 33.7 (1–92) | 4 |
| (2) Mediastinal tumor | 45 | 19 (1–96) | 40 | 2 | 1 | 2 | 8.4 (0–49) | 28 (3–98) | 15 |
| (3) Mediastinal tumor and hilar adenopathy | 8 | 17 (6–48) | 3 | 1 | 0 | 4 | 12 (6–55) | 32.5 (12–60) | 1 |
| | 75 | | | | | | | | |
| (c) Parenchymal infiltration | | | | | | | | | |
| (1) Parenchymal involvement only | 6 | 29 (4–80) | 4 | 0 | 0 | 2 | 18 (1–78) | 51 (12–102) | 3 |
| (2) Parenchymal infiltration with hilar adenopathy | 10 | 15 (4–36) | 4 | 2 | 0 | 4 | 5.7 (1–24) | 21.3 (4–36) | 4 |
| (3) Parenchymal infiltration with mediastinal tumor | 8 | 12 | 7 | 0 | 0 | 1 | 14.8 | 25.5 | 4 |
| (4) Parenchymal infiltration with hilar and mediastinal tumor | 3 | 10 (3–14) | 3 | 0 | 0 | 0 | 15 (9–20) | 25 (12–34) | 2 |
| | 27 | | | | | | | | |
| (d) Pleural involvement with or without other intrathoracic lesion | 22 | 19 (2–72) | 15 | 0 | 0 | 7 | 4.2 (0–15) | 23.8 (4–78) | 9 |
| | 214 | | 172 | 12 | 1 | 29 | | | 62 |

## CLINICAL CHARACTER

In general, the age and sex grouping conforms to other reported series. Three Jewish patients and one negro were exceptions in a racial distribution predominantly white and American-born. A few individuals were of Southern or Northern European origin. There were no Orientals and no American Indians or Mexicans.

Hereditary influence would seem to have little bearing. Less than 5 per cent had close

The outstanding initial symptom was adenopathy or tumor mass. This occurred, however, in but 50 per cent of the series. Malaise, weakness, ease of fatigue, or pruritus were the common other initial symptoms, markedly less frequent. Loss of weight, fever, anorexia, constipation, cough, or dyspnea, were associated symptoms in but one-fourth of the group. The duration of symptoms prior to admission had been predominantly less than twenty months (39.5 per cent, 1–9 months; 27.4 per cent, 10–19 months).

Generalized adenopathy or cervical adenopathy dominated the physical findings. Enlargement of spleen, or axillary adenopathy appeared in but one-fourth of the cases. Other adenopathy, abdominal tumor other than spleen, edema, or fever appeared in approximately one-eighth of the group.

tients with relatively extensive pulmonary and mediastinal involvement there was a wide variation in the red cell or white cell counts, with little variation, however, in the differential pattern.

The average (as well as minimum and maximum) periods of the duration of symptoms before admission, and the total

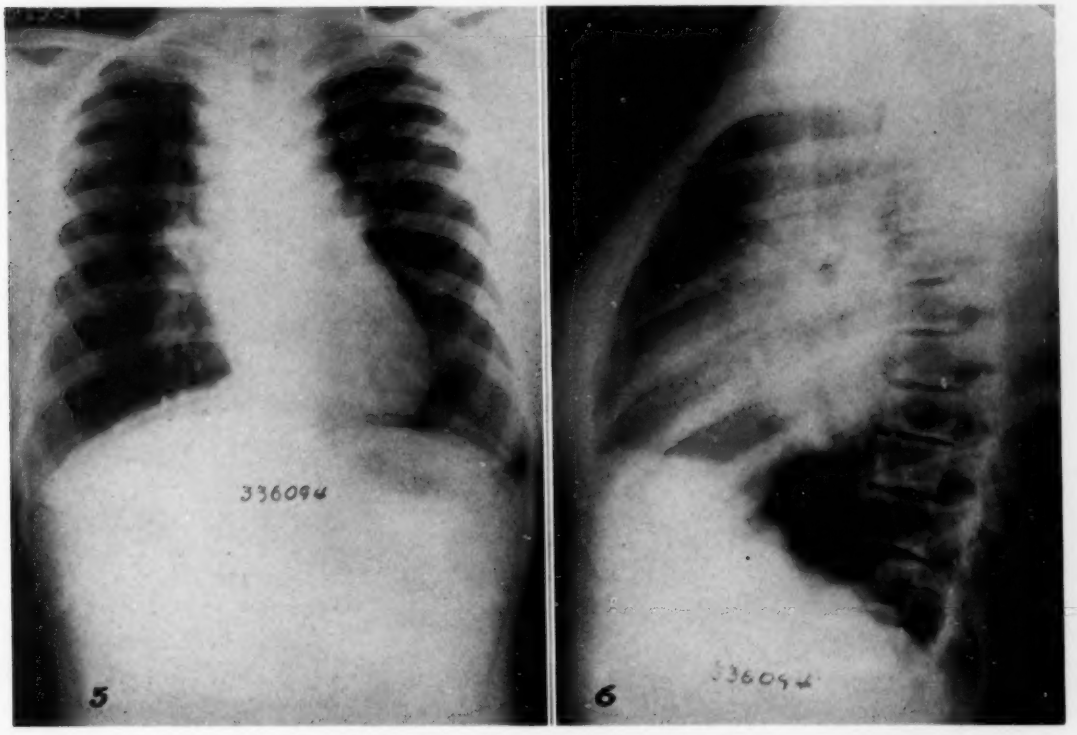



Plate III. *Hilar and Mediastinal.* No. 336094 (Serial 161). Female, aged seventeen. Weakness for four years, weight loss, chest pain, fever. Enlarged tonsils, enlarged spleen.

Fig. 5. Broadened supracardiac shadow; hilar increase. Calcareous hilar adenopathy, not affected by subsequent irradiation.

Fig. 6. Lateral: Gross pericarinal infiltration; substernal space not involved. Systemic irradiation: clinically well, fourteen months.

The predominant character of the blood was a moderate secondary anemia, occasional increase in platelets, moderate leukocytosis, relative polymorphonuclear-cytosis, reduction in lymphocytes and monocytes, with eosinophils frequently increased. Immature cells were rare. In this series no outstanding variation in blood formula differentiates the pathologic classification between Hodgkin's disease and sarcomatous Hodgkin's. In those pa-

duration of disease (from onset of first symptom to death or last report) are shown in Table III.

### ROENTGEN PULMONARY PATHOLOGY

Eighteen of the patients studied had *no initial* roentgenographic *chest examination.* Two of these were examined subsequently, with demonstration of mediastinal tumor in one, hilar adenopathy in the other. Positive biopsy evidence is available in 7 of

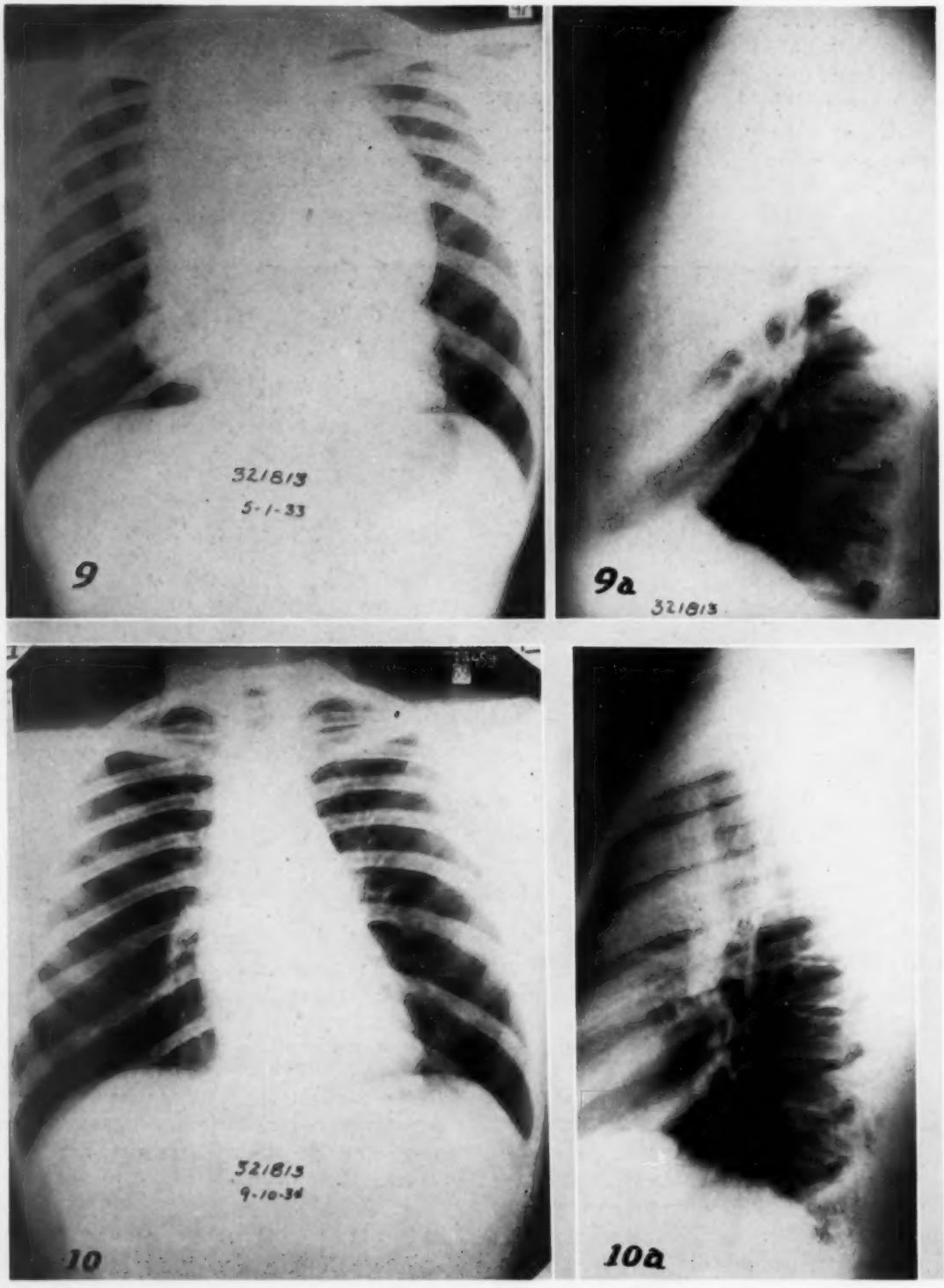



Plate iv. *Mediastinal.* No. 321813 (Serial 146). Male, aged twenty-five. Progressive swelling of neck for one year, weight loss, fatigue. Gross peripheral adenopathy. Biopsy: Hodgkin's disease.

Fig. 9. (On admission.) Gross mediastinal tumor occupying half the width of chest.

Fig. 9*a*. Lateral: Complete filling of anterior mediastinum by tumor. Systemic irradiation: Clinically markedly improved twenty-one months later.

Fig. 10. (Sixteen months after initial treatment.) Almost normal mediastinal contour.

Fig. 10*a*. Lateral: Re-aeration of substernal space—minimal pretracheal increase in soft tissue.

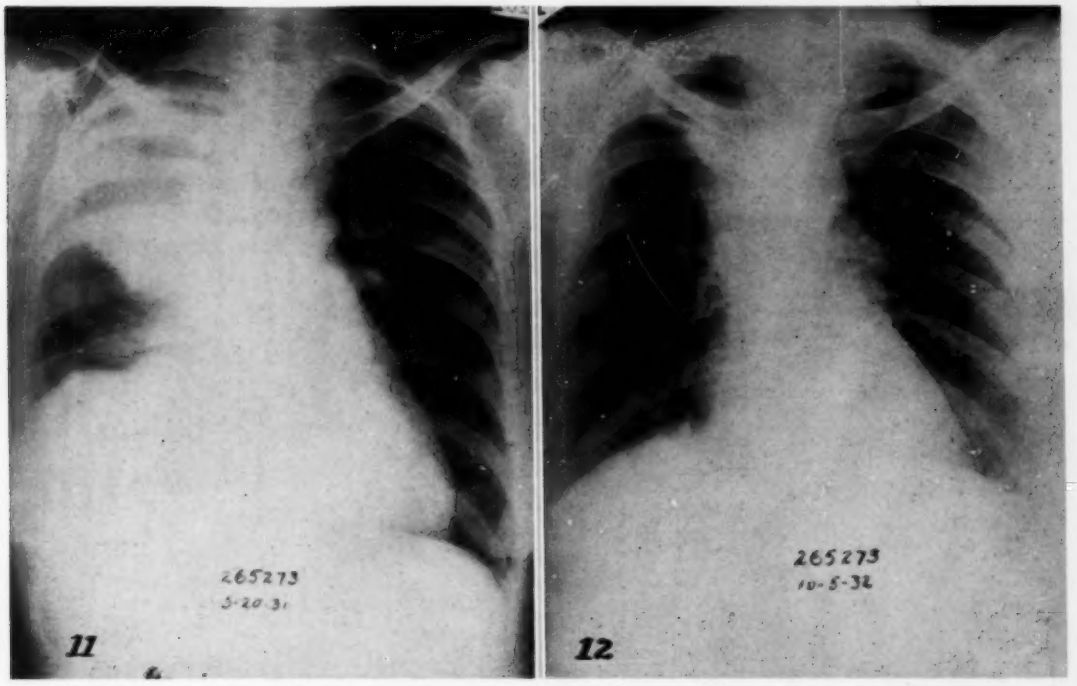



Plate v. *Parenchymatous and Mediastinal.* No. 265273 (Serial 185). Female, aged forty-four. Weakness for two years, weight loss, dyspnea, nervousness, night sweats. Admission clinical diagnosis: Bronchogenic carcinoma.

Fig. 11. Palsy of right diaphragm, infiltration of right upper lobe, partial atelectasis of right posterior lobe. Simulates primary bronchogenic carcinoma. Bronchoscopic biopsy: Negative. Lymph node biopsy: Sarcomatous Hodgkin's disease.

Fig. 12. Subtotal regression of infiltration right upper hilus. Re-aeration of lung, resumption of function of right diaphragm. Local irradiation: Clinically improved fifteen months. Death in twenty-ninth month. Autopsy: Sarcomatous Hodgkin's disease.

the remaining 16. One of this group had a known skeletal lesion.

The roentgen findings in this disease run the entire gamut from the healthy or normal lung fields to complete consolidation of a lung, no tumefaction to gross intrathoracic mass. The intrathoracic changes may be classified into four major groups:

| | Frequency in series of 198 with chest examination |
|---|---|
| (a) Normal lung fields and mediastinum | 37.4% |
| (b) Intrathoracic tumor or adenopathy | 37.9% |
| (c) Parenchymal infiltration, with or without (b) | 13.6% |
| (d) Pleural involvement, with or without (b) or (c) | 11.1% |

The further separation into subgroups, distributed, as to roentgen signs, in each pathologic classification has been shown in Table III.

(a) *Normal Lungs and Mediastinum.* The absence of roentgen signs of intrathoracic abnormality in over one-third of those examined is of importance. Biopsy proof was available in 61 patients (81 per cent) of this group. Four had known skeletal lesions, one a lymphoblastoma cutis of many years' duration. All had manifest signs or symptoms of the disease peripherally or in the abdomen.

(b) *Intrathoracic Tumor or Adenopathy.* The evidences of tumor or adenopathy in the chest ranged from the localized perihilar or carinal lymph node enlargement to gross midthoracic tumor masses occupy-

ing half the transverse diameter of the thorax. This group of more than another third presented biopsy confirmation in about the same proportion (55 cases, or 73.5 per cent) as the former.

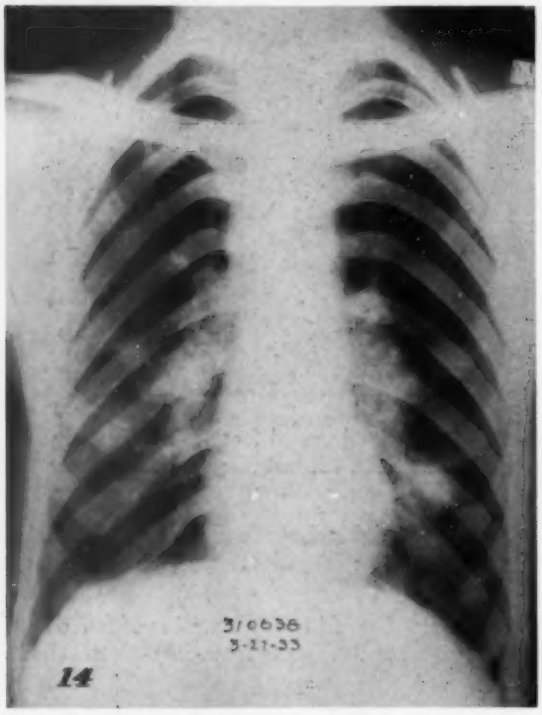
The early involvement of the hilar or mediastinal lymphoid tissue may be masked completely by the shadow of the heart and great vessels in frontal projection.

Such hilar adenopathy, especially in children (Plate 1, Figs. 1 and 2) and adolescents, has been considered evidence of glandular tuberculosis. The possibility of this type of lesion in Hodgkin's disease must be borne in mind during any consideration of differential pulmonary diagnosis. Frequently patients with Hodgkin's disease are subjected to prolonged sanatorium care because of this error of omission.

The infiltration of the mediastinal lymphoid tissue may present in frontal view no distortion of the supracardiac soft tissue. As the process continues, the earliest sign in the frontal plane is a flattening-out or loss of the curvilinear profile of the supracardiac shadow, commonly bilateral, with extension toward the thoracic inlet (Plate II, Figs. 3 and 4). If, however, this is examined in the lateral projection, the obliteration of the normally aerated substernal space is unmistakable.

As the tumefaction progresses, the pulmonary fields are displaced laterally with some tendency for the smooth homogeneous soft mass to extend along the upper bronchovascular trunks.

The midthoracic masses cannot be fully localized in frontal projection. Frequently these will be perihilar and peritracheal rather than thymic or mediastinal (Plate



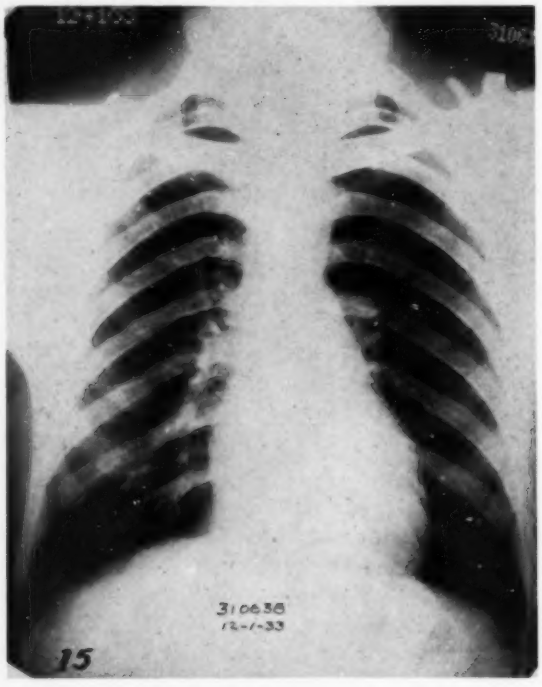




Plate vi. *Parenchymatous, Hilar and Mediastinal.* No. 310638 (Serial 192). Male, aged twenty-one. Cough, fatigue, fever. Tonsils enlarged. Generalized adenopathy. Biopsy: Hodgkin's disease.

Fig. 14. Disseminated parenchymatous involvement simulating metastatic neoplasm; hilar adenopathy; paratracheal tumor. Systemic irradiation: Marked clinical improvement.

Fig. 15. (Eight months later.) Complete disappearance of all previous lesions. Clinically well on last report; playing semi-professional baseball.

III, Figs. 5 and 6). Certain of these will be retrocardiac and associated with mild anorexia.

The contour and homogeneity of the involvement in the frontal plane may admit no differentiation of Hodgkin's disease from aneurysm, perihilar tuberculosis, or primary bronchogenic carcinoma. Laterally or oblique studies with roentgenoscopic control are advisable in the establishment of a diagnosis. The value of lateral projection in the demonstration of these masses is such that routinely we so examine any patient who presents any clinical signs suggesting lymphoblastoma. Further (Plate IV, Figs. 9, 9*a*, 10 and 10*a*) in the control of treatment, these masses first recede mesialward, continuing to occupy the retrosternal space until late in their regression. Persistent tumefaction may be entirely hidden by the sternal, cardiac, and vertebral shadows on frontal projection.

(c) The group with *parenchymal involvement*, although definitely smaller than the former, offers considerable difficulty in interpretation because of the protean character of change. The peribronchial infiltration and the parenchymal lesions may simulate acute inflammatory disease, pulmonary abscess, tuberculosis, primary bronchogenic carcinoma (Plate V, Figs. 11 and 12), or metastatic neoplasm (Plate VI, Figs. 14 and 15). Two patients presented a spontaneous palsy of the hemidiaphragm.

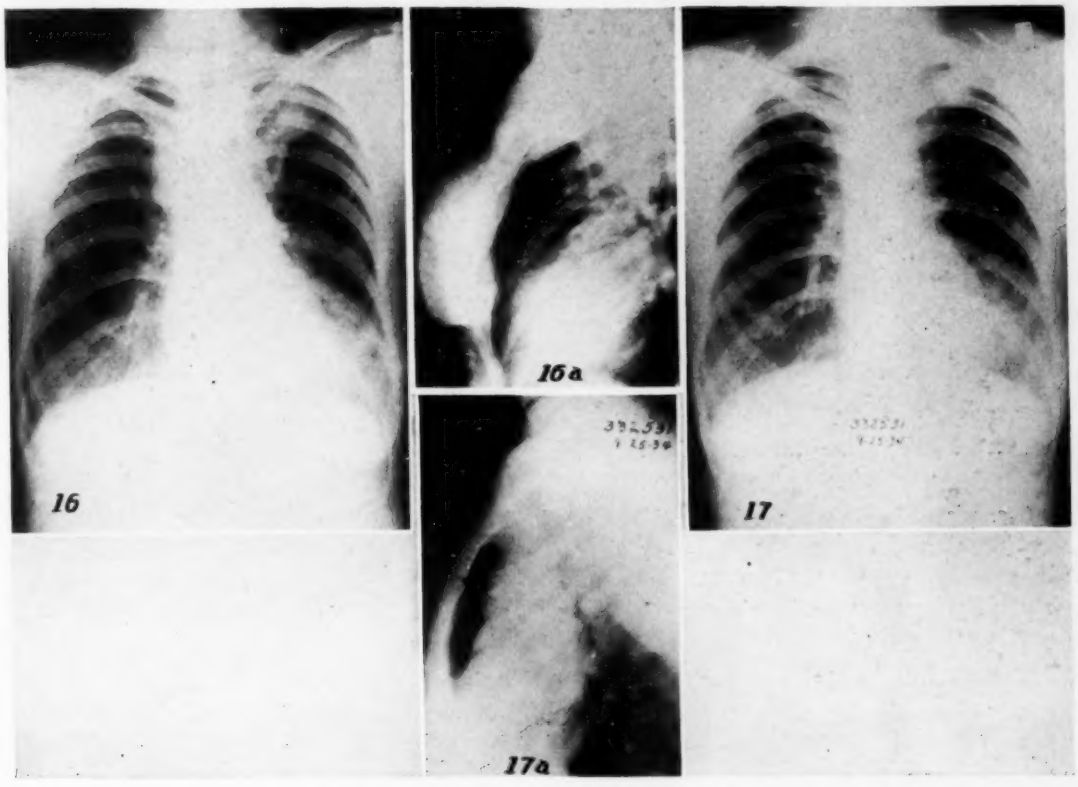



Plate VII. *Parenchymatous and Local Skeletal.* No. 332531 (Serial 176). Female, aged twenty-eight. Previously treated for some time for supposed pulmonary tuberculosis and sternal tuberculosis. Sternal mass with sinus tracts. Generalized adenopathy, pruritic skin lesions.

Fig. 16. On admission: Parenchymal infiltration left apex, hilar adenopathy, sternal mass, ?neoplasm.

Fig. 16*a*. Lateral: Detail of sternal mass. No mediastinal involvement. Biopsy of sternal mass: Hodgkin's disease. Systemic irradiation; rapid closure of sinuses; marked regression of sternal tumor.

Figs. 17 and 17*a*. After six months under treatment. Clinically well twelve months later.

One-fifth of this group presented parenchymal change only, the remainder with more or less hilar and mediastinal tumefaction. The character of the parenchymal change is at times diffuse as of an exudative nature—in others, sharply localized or nodular. The former will suggest a lobular pneumonia, or tuberculosis, the latter for employment of all possible diagnostic measures for differentiation.

A further baffling feature is the spontaneous regression of apparent widespread infiltration. Such a patient (Plate VIII, Figs. 18 and 19), near the end of prolonged, known Hodgkin's disease, had been considered and treated as a case of exudative

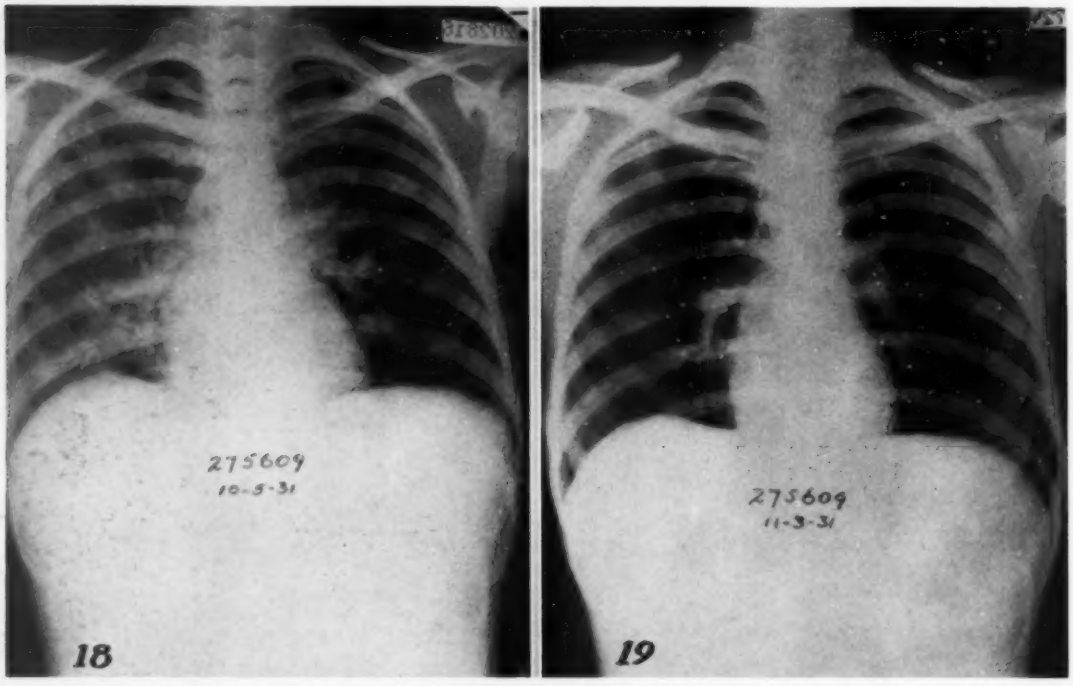



PLATE VIII. *Parenchymatous.* No. 275609 (Serial 170). Female, aged forty-six. Known Hodgkin's disease for six years. Previous roentgen irradiation. Recent weight loss, fever, pruritus, fatigue, night sweats.

FIG. 18. Admission: Disseminated small parenchymatous infiltrations, tuberculosis considered. Improvement following transfusion, sudden death in one month.

FIG. 19. Ante mortem: Complete disappearance of former infiltration. Autopsy: All pulmonary lymph nodes and follicles showed sarcomatous Hodgkin's change.

definite metastatic neoplasm (Plate VI, Figs. 14 and 15).

Such patients are often treated for supposed pulmonary tuberculosis, especially in the presence of possible contact, or with the development of sternal (Plate VII, Figs. 16, 16*a*, 17 and 17*a*) or costal involvement and sinus tracts. Absence of, or questionable bacteriologic and allergic evidence should give rise to the consideration of Hodgkin's disease.

The high number of biopsies (85 per cent in this group) is an indication of the need pulmonary tuberculosis. After several transfusions, and without irradiation, the parenchymal infiltration entirely disappeared leaving an apparently normal chest. Death occurred within a few days. Microscopic examination post mortem revealed that all lymph nodes and follicles had undergone sarcomatous Hodgkin's change. There was no evidence of tuberculosis or nonspecific inflammatory disease.

Such infiltrative manifestations have been considered suggestive of the sarcomatous type. We do not find sarcomatous

Hodgkin's disease of appreciably greater frequency in this group. Certain of these patients have shown excellent response to irradiation.

(d) *Pleural involvement* may or may not be accompanied by other intrathoracic manifestation of the disease. Pleural abnormality alone has been more common in association with abdominal Hodgkin's disease. This may or may not regress with irradiation.

Another patient, originally showing parenchymal involvement, pleural effusion, and mediastinal tumor, responded well to irradiation. Subsequently gross Hodgkin's tumefaction was observed in the pleura, without recurrence of the previous lesion (Plate x, Figs. 24 and 25).

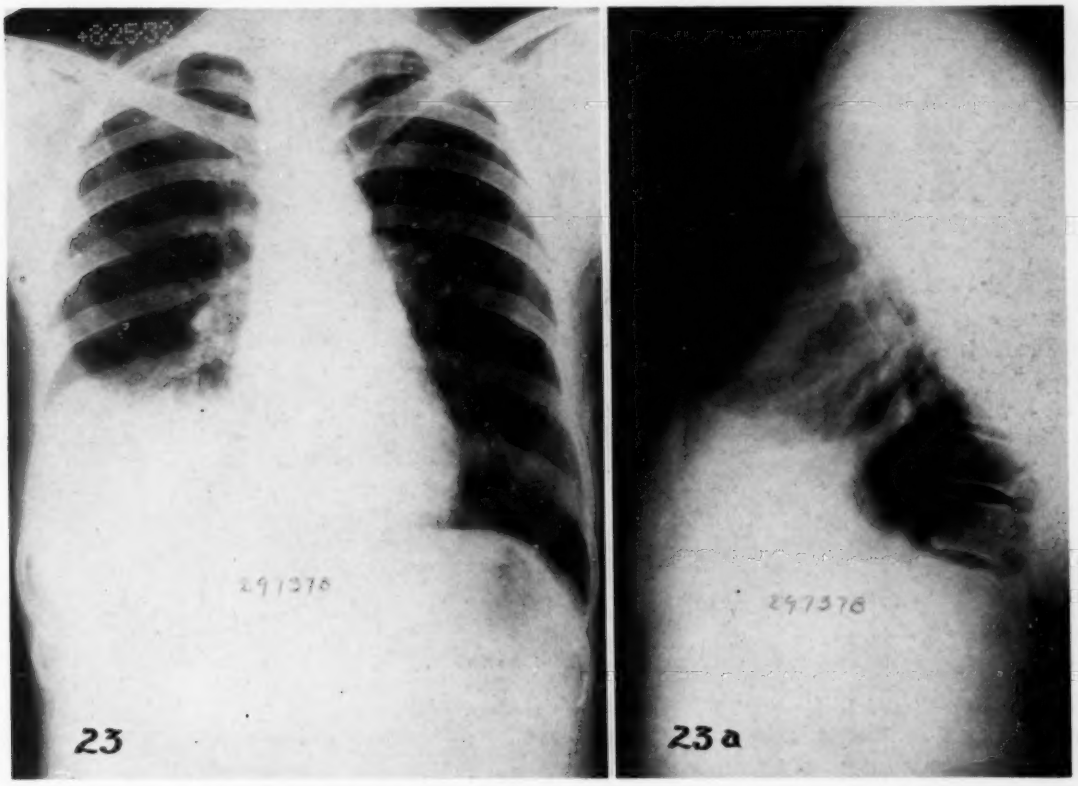



Plate ix. *Pleural.* No. 297378 (Serial 203). Female aged fifty-eight. Cough for two years, weight loss dyspnea, fever, feeling of weight in abdomen. Generalized adenopathy, enlarged liver.

Figs. 23 and 23*a*. Right pleural effusion. No pulmonary lesion.
Gastrointestinal roentgen studies revealed extra-alimentary mass in midabdomen. Pyelographic appearance normal. Chylous fluid on thoracentesis, not staining with Sudan iii. Surgical removal of tumor of jejunal mesenteric lymph nodes: Hodgkin's disease. Systemic irradiation: Clinically well ten months later.

In 2 of our patients a fluid, chylous in appearance but not staining with Sudan iii, was aspirated (Plate ix, Figs. 23 and 23*a*).

Bizarre distortion of the diaphragm by subphrenic tumor may appear.

Pleural reaction of obscure origin suggesting either effusion or tumefaction, with or without other intrathoracic lesion, must suggest to the roentgenologist the possibility of lymphoblastomatous change.

Positive microscopic diagnosis was available in 19 (86 per cent) of this group.

## GENERAL COMMENT

Although an abdominal mass was present in several, and symptoms referable to

the gastrointestinal tract presented in more than one-third of the entire series, no evidence of gastric wall lesion was found in the 21 patients to whom a barium meal was given. In the autopsied cases no record is made of a gross gastric lesion. Involvement of the mesenteric and retroperitoneal nodes was common in the necropsy material.

Eleven patients had skeletal lesions discovered prior to necropsy.

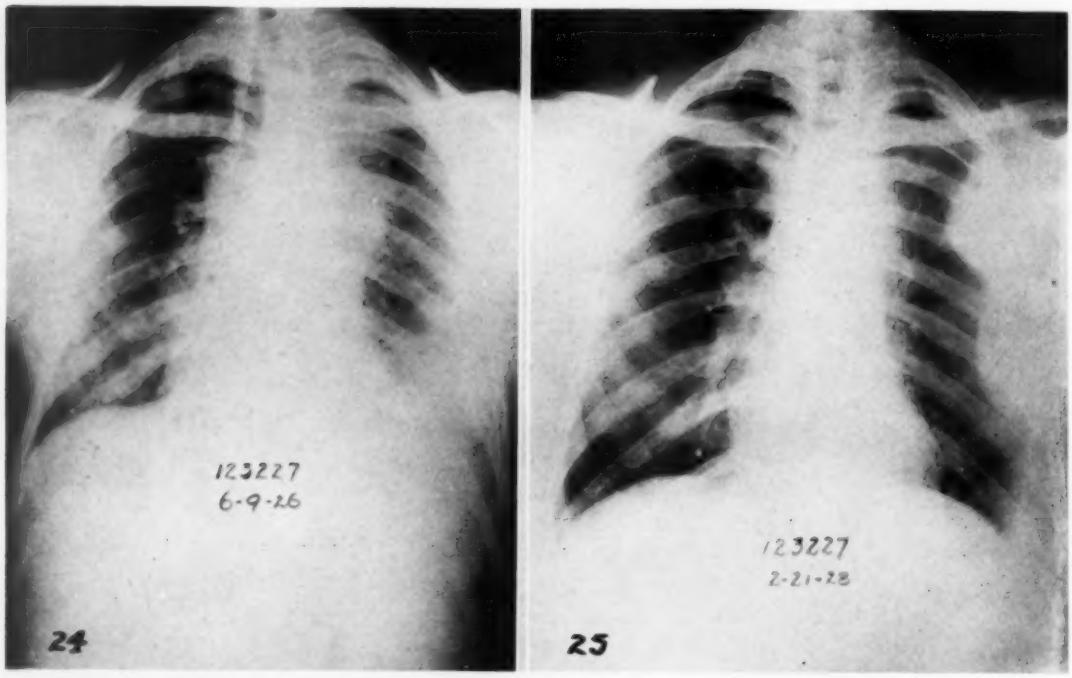



PLATE X. *Pleural and Mediastinal.* No. 123227 (Serial 121). Male, aged twenty-nine. Enlarged glands in neck two months. Weight loss, fever, nausea, and vomiting. Generalized adenopathy.

FIG. 24. Mediastinal tumor; left pleural effusion. Temporary improvement with multiple local irradiation.
FIG. 25. Twenty months later, return of symptoms, regression of mediastinal tumor; resolution of pleural effusion; new nodular pleural involvement. Death in a few months; no autopsy.

## SUMMARY

In this series of 214 cases, the clinical symptoms or signs and the changes in character of the blood often suggest this disease. They are not indicative of the extent of the intrathoracic involvement.

Commonly, roentgenographic evidence of intrathoracic tumor, adenopathy, or parenchymal infiltration is far greater than the clinical signs or symptoms of intrathoracic abnormality would indicate.

There is no uniformly pathognomonic roentgenographic sign of the Hodgkin's type of lymphoblastoma within the thorax. Virtually all common changes may be encountered.

Consideration of the Hodgkin's type of lymphoblastoma cannot be eliminated in many instances from the differential diagnosis of pulmonary disease.

Roentgenologic appearance offers no criteria for prognosis as to the duration of the disease.

More than one-third of the patients in this series had a roentgenologically normal chest.

In the remaining cases the roentgen examination of the chest offered the best opportunity, short of pathologic study, for the diagnosis of the disease and its extent.*

* For discussion see page 179.

Vol. 36, No. 2

# ROENTGENOLOGIC CONSIDERATIONS OF LYMPHOBLASTOMA

## II. ROENTGEN THERAPY OF HODGKIN'S DISEASE*

*By* HAROLD W. JACOX†, B.S., M.D., CARLETON B. PEIRCE, A.B., M.S., M.D., *and* ROSCOE C. HILDRETH, M.D.

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IN AN attempt to evaluate irradiation methods in the treatment of Hodgkin's disease, the experience of this department during the past decade has been surveyed.

The cases reported in the preceding paper (Peirce et al.) may be separated into four groups, almost equal in number, on the basis of method of treatment:

Group I: Fifty-eight patients received repeated local irradiation.

Group II: Fifty were irradiated over the entire lymphatic system.

Group III: Fifty-three had only one or two local treatments.

Group IV: Fifty-four received no treatment in this hospital.

The major number of patients in Group I were seen during the first half of the decade, the cases in Group II chiefly during the second half. Groups III and IV are distributed throughout the entire period, less of Group III in the last five years. The majority of these patients had had symptoms for an average of one and one-half years.

Approximately an equal percentage of each group had received irradiation before admission.

### TECHNIQUE

In Group I, local irradiation was applied repeatedly to the areas manifestly involved with either medium or short wave length roentgen rays. A dosage of 100–400 roentgens per portal, at intervals of approximately one month, in many cases was administered during a period of a year or more. Only two or three areas were treated in one course. The deep-seated glands, except the mediastinal, were rarely irradiated.

The literature indicates that the majority of roentgen therapists use this method.[3]

In Group II, general systemic irradiation, including all lymph-gland-bearing areas, was employed, with medium wave length to the peripheral glandular structures and short wave length roentgen rays to the deeper glands of the chest, abdomen, and pelvis. In children, medium wave length was used throughout. The dosage varied from 200–500 roentgens per field, depending upon the patient's age, his clinical condition, and blood findings. Twelve to fifteen portals, usually one or two per day, constituted each course. A second similar course was usually given after four or six weeks, unless the patient showed an exceptionally good response. This is the method favored by Desjardins[1] and Gilbert.[2] Further irradiation was administered only when there were signs of activity of the process, and then confined to the evident active areas. In a few instances, as many as three or more such courses of irradiation were administered.

When a local region of increased intensity of disease presented, the dosage over such an area was customarily increased without other change in the technique or general routine. When the extent of the involvement and the generally poor condition of the patient precluded the expectation of other than a temporarily palliative effect, such a result was sought by means of a reduced dosage over all areas.

The irradiation in Group III at this hospital was obviously incomplete. These patients were too ill for the usual regimen,

* From the Department of Roentgenology, University of Michigan. Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

† Now residing in Pittsburgh, Pa.

wished to be treated at home, or did not continue the projected regimen for various reasons.

The patients in Group IV are considered only as controls, since they received no irradiation in this department.

### CLINICAL RESULTS

A comparison of the initial clinical response, within four to eight weeks after treatment was begun, is shown in Table I. Recession of tumor or adenopathy occurred in about the same percentage in Groups I and II. With systemic irradiation, twice as many patients lost their presenting symptoms as did those with repeated local irradiation. A sense of well-being was more frequent in the generally irradiated group. Subsidence of fever and gain in weight were also more common. Certain patients, whose condition became refractory to repeated local treatment, showed definite improvement when given general irradiation.

TABLE I

INITIAL CLINICAL RESPONSE
(4–8 weeks)

| Group I Repeated Local Irradiation | | Group II General Systemic Irradiation |
|---|---|---|
| 66% | Recession of tumor | 63% |
| 15% | Loss of presenting symptom | 30% |
| 9% | Feeling of well-being | 14% |
| 6% | Loss of fever | 20% |
| 7% | Gain in weight | 16% |

At the end of three months, the clinical advantage of the systemic method was even more apparent. When last seen, 27 per cent of Group II, but only 7 per cent of Group I were considered clinically well. Forty-one per cent of Group II were clinically improved, as compared with 28 per cent of Group I.

Radiation sickness was no more prevalent, nor blood changes more marked with general irradiation, than after repeated local treatment.

With repeated local irradiation, the adenopathy usually showed regression. However, upon return visits, few patients had a sense of well-being and new areas often showed involvement.

No conclusions can be drawn from the clinical response in Group III because of the great variability in dosage, the interval at which treated and the short period of observation.

The clinical course of the patients in Group IV was generally downhill.

Patients with increased temperature, toxic skin manifestations, generalized pruritus, pain and intermittent swelling of the lower extremities, customarily refractory to the method of treatment in Group I, were usually relieved by the systemic irradiation.

Several patients have lived comfortably for as long as ten years or more, even though localized evidence of the disease remained apparent. The exceptional case, which does well with little or no treatment, will appear in any similar number of patients.

Irradiation, even in small amounts, seemed uniformly beneficial rather than deleterious.

### DURATION OF DISEASE (KNOWN DEATHS)

An analysis of the known deaths which have occurred in this series is shown in Table II. The smaller number of cases in Group II, who had systemic irradiation, is logical, since this type of treatment has been employed only during the last five years. The figures represent the arithmetic mean duration of disease expressed in months. It is interesting to note that when the various groups are compared, there is a close similarity in duration of symptoms prior to admission. The exclusion of the exceptional cases does not materially disturb the relative proportion of the averages in each group.

The period of our observation of the patients in Groups I and II is virtually identical.

Of those cases in which known date of death provides an absolute gauge of total

duration of disease, irradiation before first admission to this clinic has not materially affected group averages.

Perhaps the total duration of disease, as positively determined by death and by survival under observations, is not the most desirable criterion by which to judge efficacy of radiation therapy.

figures. Further, these patients were reported clinically well on last contact.

## DISCUSSION

It is, as yet, too soon to hope that any one of these methods has effected permanent cure. Our experience, however, indicates that systemic irradiation will afford

TABLE II

KNOWN DEATHS

(Averages in Months)

| No. of Cases | Type | Duration of Symptoms Prior to Admission | Period of Observation | Total Duration of Disease | (Minimum-Maximum) |
|---|---|---|---|---|---|
| 24 | Group I (Repeated local irradiation) | 16 | 21 | 38 | 9–126 |
| 8 | Group II (Systemic irradiation) | 17 | 23 | 41 | 8– 77 |
| 14 | Group III (Occasional local irradiation) | 18 | 2 | 22 | 5– 50 |
| 16 | Group IV (Untreated) | 12 | 1 | 11 | 4– 81 |

However, the average total duration of the disease in all treated cases (Groups I, II and III) is twice that of the group which received no irradiation at any time (Group IV). Such factual evidence can scarcely be ignored.

Upon the basis of the period of survival, as determined by death, there appears to be little choice between method one and method two. It must be admitted that the systemic irradiation has not materially lengthened the duration of life after onset of symptoms, as compared with the repeated local irradiation.

Many patients treated by the second method during the last five years are still living and under observation. It is legitimate, therefore, to gauge probable extent of life among these individuals, even though the disease has not yet been terminated by death. Judged on this basis, twice as many individuals in Group II as in Group I have already survived the expected life span as determined by the death

greater comfort throughout the remaining period of the patient's life.

Analysis of initial symptoms has shown that cough, dyspnea, icterus and edema are uncommon in the presence of roentgenographic evidence of pulmonary infiltration, mediastinal or retroperitoneal tumors. Frequently, on first examination, the patient has symptoms, as well as adenopathy. With this in mind, delay of treatment until there is manifest distress is not warranted. Immediate treatment should be given if the most satisfactory palliation is to be expected.

In our concept of Hodgkin's disease as a neoplasm involving the entire lymphopoietic system, irradiation of all lymphoid areas is advisable.

## CONCLUSIONS

From a survey of the clinical results of irradiation in 161 cases of Hodgkin's disease within the past decade, we may conclude that:

1. No unfavorable biologic changes were observed following irradiation by any of the methods employed.

2. Roentgen therapy in any degree has induced definite extension of life, as compared with the untreated patients.

3. Systemic irradiation has been no more effectual than repeated local irradiation in prolongation of the total duration of the disease in those cases now known to have died.

4. Future figures, more favorable to systemic irradiation, derived from that group of patients still under observation, and who have already exceeded the life span as determined from the known dead, may be expected.

5. Systemic irradiation of all lymphoid areas is the method of choice, in the light of symptomatic response.*

* For discussion see page 179.

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Vol. 36, No. 2

# UNUSUAL COMPLICATIONS OF LYMPHOBLASTOMA AND THEIR RADIATION TREATMENT*

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HODGKIN'S disease or lymphosarcoma, especially when the disease primarily involves the abdominal nodes, is much more common than is generally realized. A great many cases are constantly being overlooked or mistaken for other disturbances with which hyperplasia or inflammation of lymphatic structures may be associated. By their tendency to invade different groups of lymph nodes in different parts of the body or to infiltrate any structure in which lymphoid tissue is normally present, or even structures in which lymphoid tissue normally does not occur, these varieties of lymphoblastoma may simulate almost any disease. Many physicians have the impression that the manifestations of lymphoblastoma, especially the enlargement of lymph nodes, always begin in the cervical nodes and thence extend to the mediastinal, retroperitoneal, and other nodes. This is true for the majority of cases, but in an important minority the disease first affects the abdominal, mediastinal, or inguinal nodes and later spreads to other nodes. Enlargement of retroperitoneal nodes as the initial lesion of the disease is fairly common.

## ETIOLOGY

Rapidly accumulating evidence indicates that in close association with, or as a possible etiologic factor in Hodgkin's disease and lymphosarcoma is chronic infection of any kind; pyogenic in most cases, tuberculous in a small percentage of cases, syphilitic in an occasional case. In other words, it is possible that any variety of chronic infection may give rise to lymphoblastoma in persons predisposed by a hereditary tendency to lymphoid disturbance. Evidence suggesting that chronic infection is the immediate cause of lymphoblastoma is to be found in the circumstance that, when the history of the patient's illness is carefully recorded and when his medical antecedents are subjected to a systematic inquiry, the group or groups of lymph nodes that first enlarged usually are anatomically related to a region in which chronic infection has been present for months or years. Since long standing infection of teeth, tonsils, or sinuses is so common, this probably explains why, in the majority of cases, the disease starts in the cervical nodes. On the other hand, chronic infection of teeth, tonsils, or sinuses, chronic cholecystitis, chronic appendicitis, chronic inflammation of the urinary tract or of the genital organs, may possibly explain why, in a considerable proportion of cases, lymphoblastoma originates in the abdominal nodes, whence it extends to the mediastinal, inguinal, cervical, and other nodes.

## COMPLICATIONS

During the extended course of the disease a great variety of complications may develop. It is precisely because of the protean character of these complications that lymphoblastoma may simulate many other conditions and thus may tend to make diagnosis difficult. Among these complications may be mentioned fever; pruritus; discrete or diffuse infiltration of the skin, which may be associated with pruritus or which may occur independently; infiltration of the orbital (periocular) tissues or of the eyelids, with or without impairment of vision; erosion and sometimes actual necrosis of the sternum by enlarging lymph nodes in the mediastinum; injury to the recurrent laryngeal nerve by pressure from

* Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

adjacent, hyperplastic nodes or by actual, lymphoblastomatous infiltration of the nerve; pleural effusion from obstruction of the great vessels in the mediastinum; ascites from vascular obstruction by enlarged nodes in the mesentery or in the retroperitoneal spaces; edema of the lower extremities by vascular obstruction in the iliac or inguinal regions; infiltration of the testis; involvement of bone by direct erosion or by invasion of the marrow; infiltration of the spinal canal and secondary lesions of the spinal cord; infiltration of the brain, and secondary infection associated with lymphoblastoma. This enumeration is based on cases actually observed. Some of these complications have been seen in many cases, while others have been known to occur only in a few instances. This incomplete list may serve to give an idea of the varied character of the complications that may be encountered in lymphoblastoma.

When we undertook to write on this subject the intention was to consider from the clinical and therapeutic standpoints all the complications mentioned, but it soon became apparent that such a task was altogether too ambitious for a single paper. Therefore, we have found ourselves obliged to limit the scope of this paper to a few complications which seem especially interesting.

*Fever and Pruritus.* Fever and pruritus, with or without toxic or infiltrative lesions of the skin, indicate lymphoblastomatous invasion (Hodgkin's disease or lymphosarcoma) of the abdominal (retroperitoneal) nodes. Why this should be so remains an unsolved problem, but that it usually is so is proved by the fact that both the fever and itching, and the cutaneous lesions also when these are present, usually diminish rapidly after thorough irradiation of the abdomen, whereas such a favorable effect is not observed after irradiation of other regions. Enlarged retroperitoneal nodes may or may not be readily palpated. This depends on the degree of enlargement of the nodes, on the muscular development and tone of the abdominal wall, on the ability of the patient to relax, and on the skill of the examiner. When individual nodes cannot be felt in the epigastric region and on each side of the spinal column, a sensation of undue resistance and tenderness on deep pressure is commonly obtained. This finding is usually bilateral, but the lymphadenopathy may be more pronounced on one side than on the other. Sometimes, in fact, enlarged nodes on the left side may form a mass that may deceive one into assuming that he is palpating an enlarged spleen instead of a mass of hyperplastic lymph nodes; or, if the mass is situated high on the right side, it may erroneously be thought to represent the liver. Sometimes, also, the anterior, inferior border of the liver may be abnormally low, and it may be assumed that the liver has become infiltrated by the lymphoblastomatous process. Hepatic infiltration or metastasis does occur in some cases, usually late in the course of the disease; in the majority of cases, however, the liver is probably not affected but is pushed forward and downward by enlarged retroperitoneal nodes crowding the posterior part of the organ upward and forward. Evidence to support this view is to be found in the fact that, as the retroperitoneal nodes retrogress after thorough irradiation, the liver rapidly resumes its normal position.

The foregoing physical indications of lymphoblastomatous hyperplasia of the retro-abdominal nodes are often associated with more or less telltale symptoms, such as an increasing sensation of fullness in the epigastrium after even a moderate meal, an increasing tendency for gas to accumulate in the bowel, with belching or abnormal flatulence or both, and increasing constipation and vomiting. The presence of any or all of these symptoms, even when enlarged abdominal nodes cannot be palpated, might suggest enlargement of these retro-abdominal nodes. By themselves, however, they are not conclusive. The most significant feature is the gradual increase of these symptoms.

Case 1. The patient, a man, aged sixty-three, who registered at The Clinic on April 11, 1935, had for years suffered from headache, so-called attacks of "biliousness," indigestion, and constipation, and from frequent periods of exhaustion ever since his marriage. This indigestion always had come on soon after eating, had been accompanied by gaseous distention, had been made worse by food and had never been relieved by soda. It had also been accompanied by a burning sensation around the stomach and by a sour taste. He had spent much time at various health resorts. Three times in his life, once when a young man, once in 1918, and once in 1931, he had had three attacks of rather severe pain in the lower part of the abdomen, and for this he had been given morphine, with relief. In 1931 his appendix and gallbladder had been removed; this had been followed by relief from constipation and by improvement in digestion. Early in 1932, his health again had slumped and a corneal ulcer had developed; treatment with typhoid vaccine had been successful. In 1933, the strain of business conditions again had caused his health to deteriorate. In the spring of 1934, he had noticed a gradual thickening, first of the lower lid and later of the upper lid, of both eyes. This had been accompanied by photophobia. For many years he had been troubled by a disease of the skin, characterized at first by macular and later by papular lesions, but recently this had been accompanied by marked itching and had been called urticaria. In January, 1935, chills, fever, and night sweats, accompanied by nausea and vomiting, had developed. A second, similar "attack" had occurred in February, 1935.

Physical examination disclosed thickened eyelids with impairment of vision, apparently from conjunctival edema, slight enlargement of the cervical, axillary, and inguinal lymph nodes on both sides, and increased resistance and a doughy sensation on palpating the upper part of the abdomen, suggesting enlarged retroperitoneal nodes. Careful palpation of the relaxed abdomen enabled one to feel definitely enlarged nodes in the epigastric and umbilical regions as well as along each side of the spinal column. Microscopic examination, by Broders, of a lymph node removed from the left axilla revealed lymphosarcoma. Even without biopsy, however, the general lymphadenopathy pointed to lymphoblastoma, and the long-continued fever and pruritus were almost certain indications of lymphoblastomatous invasion of the abdominal (retroperitoneal) nodes.

On April 20 and 21, 1935, the periocular infiltration was treated with radium; 6,270 mg-hr. of radium irradiation was given to both eyes in the form of a surface pack. Between April 22 and May 2, 1935, both sides of the neck and the entire abdomen were exposed to roentgen rays generated at 135 kv. (peak), filtered through 4 mm. of aluminum (neck and anterior surface of abdomen) and 6 mm. of aluminum (posterior aspect of abdomen), at a focal-skin distance of 40 cm., each of the two cervical and four anterior abdominal fields receiving 5 ma. for eighteen minutes (558 r in air) and each of the four posterior abdominal fields receiving 5 ma. for twenty-eight minutes (560 r in air).

The patient's condition improved rapidly. By the time the combined course of treatment was completed, the infiltration of the eyelids and edema of the conjunctiva had diminished to such an extent that he could read a newspaper. Since then the eyes have returned to normal, the fever and itching have subsided, and the general health of the patient has improved greatly.

In this case the disease had probably been present much longer than the patient or his attending physicians realized. The cutaneous manifestations from which he had suffered for many years are strongly suggestive, if not absolutely conclusive, on this point. In fact, the tendency to recurring periods of ill health may have been directly related. Moreover, the disease had probably begun in the abdominal nodes, and chronic appendicitis or cholecystitis may well have been the immediate etiologic factor. If more information were available about the condition of the appendix and gallbladder at the time these organs were removed, the relationship might be more definite.

In irradiating the abdomen it is a common practice to expose this part of the trunk through one anterior and one posterior field. But when, as in lymphoblastoma and certain other neoplastic processes it is essential to include all the lymph nodes from the diaphragm down to and including the groin, this can be accomplished much

more effectively by dividing the anterior aspect of the abdomen (from xiphoid cartilage to groin) into four fields, with the navel as a center, and by dividing the posterior aspect into four additional and corresponding fields. The several beams of rays should then be made to converge toward the median line, where most of the nodes are situated. Thus, not only are the abdomen and its contents more uniformly irradiated, but the effect of many converging beams of rays on the lymphoblastomatous process and its clinical manifestations is much greater than when only one anterior and one posterior field are exposed.

*Infiltration of Periocular Tissues.* Instead of infiltrating the eyelids, as in this case, lymphoblastoma sometimes infiltrates the periocular tissues within the orbit. This may cause the eyeball to protrude and vision may be more or less impaired. In such cases palpation around the eyeball usually elicits the sensation of nodular masses. Irradiation of the entire orbit and its contents, without any attempt to protect the eyeball, is followed by rapid improvement, and normal conditions are usually restored within two or three weeks. Of course, the quantitative dose to each orbital field should not exceed 80 per cent of the tolerance limit of the skin of the eyelids and of the conjunctiva. A dose larger than this might cause conjunctivitis and, especially in children, might lead to degeneration of the crystalline lens (cataract) which might not become apparent until two or three years later.

CASE II. Prior to July, 1934, the health of this patient, a woman, aged fifty-six, who registered at The Clinic on February 15, 1935, had always been good. She had then become distressed by abdominal discomfort which she described as "stomach ache." This was situated in the lower part of the abdomen and was not associated with chills, fever, nausea, vomiting, or diarrhea until the middle of September. At that time a roentgenologic examination of the gastrointestinal tract had been said to reveal that the walls of the ascending colon were abnormally thick. Medication had been prescribed, and dietary changes involving a restriction of certain meats and sugar had been advised. Her condition had improved until December, when the abdominal distress had returned and her weight had gradually decreased. The abdominal distress was of the nature of a dull, gnawing ache, mainly in the right lower quadrant. Her general condition had deteriorated, her strength had diminished, and she had begun to vomit. The pain and vomiting were not related to meals, but a cup of milk or tablets of milk of magnesia gave partial relief. The vomited material never contained blood but at times it was brown and resembled coffee grounds. Constipation was an old affair. Jaundice had never been noticed. She had lost about 30 pounds (13.6 kg.) in three months. On account of what had been called lumbago, all her teeth had been extracted several years previously. Another roentgenologic examination, ten days before her arrival at The Clinic, was said to have shown a mass in the stomach.

On physical examination at The Clinic, palpation of the abdomen elicited the indefinite sensation of a mass in the epigastric region, with tenderness; the mass did not move appreciably with respiration. Examination of the lungs, heart, pelvis, rectum, and extremities gave negative results. A roentgenologic examination of the stomach on February 18 revealed an extensive filling defect in the prepyloric and pyloric portions of the stomach (Fig. 1).

On February 22, 1935, an exploratory laparotomy was performed. On the posterior wall of the stomach, and extending posteriorly, where it had perforated against the pancreas, the surgeon found a lesion which appeared to be a carcinoma. The lymph nodes in the gastrocolic and gastrohepatic portions of the omentum were greatly enlarged. One of these nodes was removed and microscopic examination showed lymphosarcoma, grade 4. No further surgical procedures were attempted but, between March 4 and 14, a course of roentgen treatment was directed to the entire abdomen through four anterior and four posterior fields, and the neck also was irradiated because nodes in the left submaxillary triangle, which had not been felt before, were rapidly enlarging. The patient's condition soon began to improve, the abdominal pain and vomiting disappeared, and her weight and strength increased rapidly. A second roentgenologic examination, on April 22, showed marked improvement in the appearance of the stomach (Fig. 2). Between April 23 and 27 the patient received a second course of roentgen irradiation similar to the first.

The patient's condition continued to improve for about two weeks, when pain around the stomach and in the lower part of the abdomen reappeared. Abdominal palpation enabled one to feel numerous enlarged nodes; the axillary nodes also were involved. A roentgenologic examination on June 3 (Fig. 3) revealed an infiltrating lesion of the upper half of the posterior wall of the stomach and what appeared as areas of ulceration. Another course of roentgen irradiation, similar to the two previous courses, was given between June 4 and 10. Although the patient's weight increased slightly and the abdominal pain diminished for two weeks, her condition soon began to deteriorate

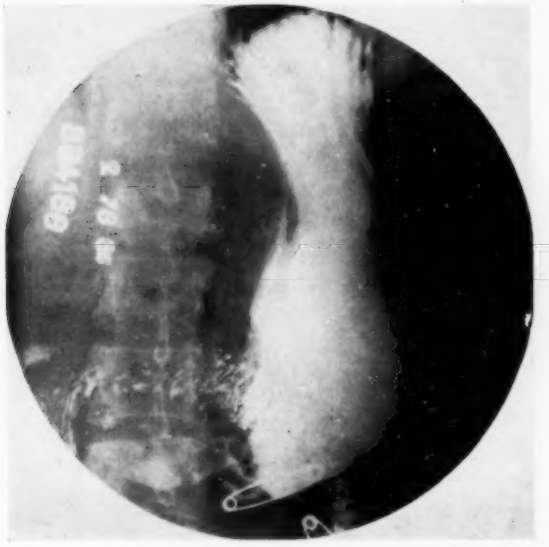

Fig. 1. Case 11. Roentgenogram of the stomach February 18, 1935. Large filling defect in the prepyloric and pyloric portions of the organ.

once more. A fourth course of treatment to the abdominal, axillary, and cervical nodes was not followed by more than slight, transient improvement. Since then, her condition has slowly been growing worse, and death seems only a question of a short time.

From the history and clinical circumstances it seems likely either that the disease had been present much longer than the patient realized or that it has been more acute than in the average case. In cases in which the disease is relatively acute, its course tends to be much more rapid and short than in cases in which the disease is more chronic. In the latter cases, as is well known, the lymphoblastomatous

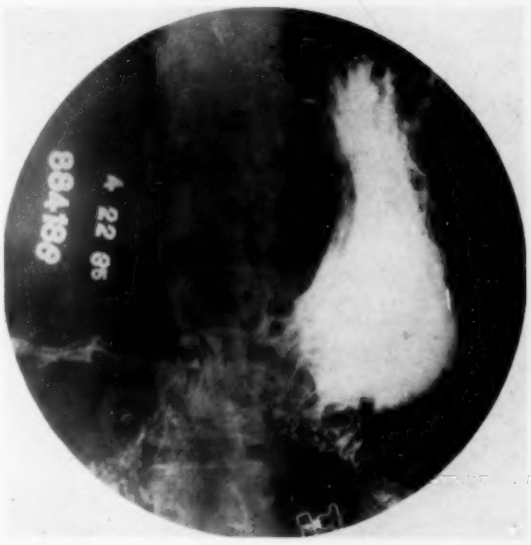

Fig. 2. Case 11. Roentgenogram of the stomach April 22, 1935. Large filling defect in the prepyloric and pyloric portions of the stomach. Some of the barium passes through the region, however, and the patient's symptoms have improved considerably.

process may continue for many years, especially when the patient receives thorough and systematic treatment. Moreover, the more acute the disease, the less effective is radiotherapy.

*Abdominal Lymphoblastoma Simulating*

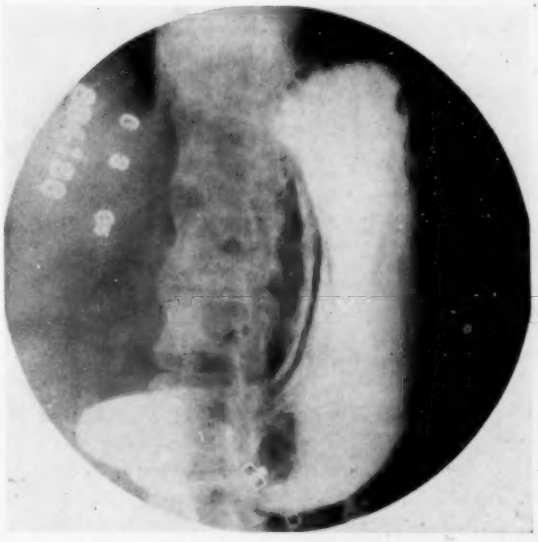

Fig. 3. Case 11. Roentgenogram of the stomach June 3, 1935, showing marked diminution in the gastric filling defect. The condition of the patient has improved a great deal.

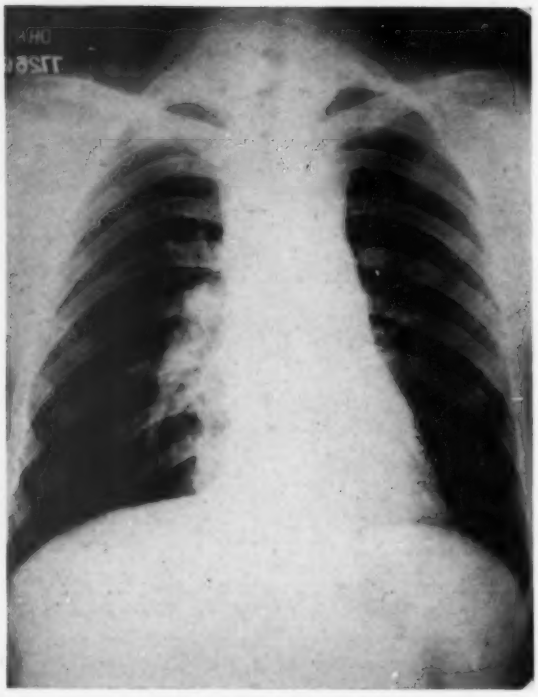

FIG. 4. Case III. Roentgenogram of the thorax February 23, 1931. Moderate widening of mediastinal shadow with apparent enlargement of some of the lymph nodes in the hilus of the lung, especially on the right side.

*Ulcer.* Occasionally, lymphoblastoma may be confined to the abdomen for some time, and the symptoms may strongly suggest gastric or duodenal ulcer. Such cases often are subjected to laparotomy on the clinical assumption of ulcer, and only when the pathologist examines sections of tissue removed from the affected stomach or duodenum, or from nearby nodes, is the lymphoblastomatous character of the lesion revealed. Some time later, other nodes in the mediastinum, neck, axilla, or groin may enlarge and thus furnish additional evidence. If space were available, several cases of this kind might be recorded.

CASE III. For years this patient, a man, aged twenty-three, who registered at The Clinic on February 23, 1931, had had frequent respiratory infections, with cough. About eight months prior to his registration in The Clinic he had noticed enlarged lymph nodes on the right side of the neck and a physician had told him that these were tuberculous. About three weeks before, another physician had removed a node from the right supraclavicular region and had submitted it to a pathologist, who had interpreted the sections as representing Hodgkin's disease. A roentgenogram of the thorax also had been made, and the patient said he had been told that the enlargement of the cervical nodes was caused by a tumor in the thorax. He then had received two roentgen treatments to the thorax but none to the neck. According to him, this had been followed by prompt and substantial reduction in size of the enlarged nodes. At no time had he lost any weight, but slight exertion had caused him to become unduly fatigued. He still complained of nasopharyngeal discharge and a paroxysmal cough, without hemoptysis. The gastrointestinal tract functioned normally.

On examination, moderately enlarged nodes were found in the right submaxillary and right supraclavicular regions, as well as on the left side of the neck, in both axillae, and both groins. The mucous membrane of the nose and nasopharynx presented evidence of chronic inflammation and was covered with purulent discharge. A roentgenogram of the thorax, taken February 23, 1931, showed moderate widening of the mediastinal shadow (Fig. 4). The patient was quite certain that the cervical nodes were much smaller than they had been before the thorax had been irradiated. The condition was clearly one of lymphoblastoma.

Between February 23 and March 3, roentgen irradiation was directed to both sides of the neck, to both axillae and groins, as well as to the mediastinum (two anterior and two posterior fields), and to the lower thoracic and lumbar regions from behind. The technical conditions of irradiation were much as in the previous case. When the patient returned, on April 13, 1931, the previously palpable nodes had disappeared, the cough and dyspnea had greatly diminished, and his general condition was excellent. He was still weak, but his strength had gradually increased. Occasional pain around one hip pointed to enlarged retroperitoneal nodes in the lumbar region. A second course of treatment, similar to the previous one, was given between April 14 and 17, 1931.

In June, 1931, the patient's condition was excellent, his former symptoms had disappeared, and his strength had continued to increase. A thoracic roentgenogram, on June 9, 1931 (Fig. 5), revealed what was regarded as infiltration of the central portion of both lungs.

On this occasion treatment was not given; the patient was instructed to return in three months. In October, 1931, with the exception of an occasional cough in the morning, the patient was as free from symptoms as from evidence of lymphadenopathy and treatment was not required.

When the patient was again examined, in June, 1932, a few small nodes could be felt in the left axilla and groin. He still complained of tiring easily and had been afraid to go back to work, but since he had been receiving $50.00 a month from an insurance company this may have been a strong deterrent to labor. At any rate his appearance was that of perfect health.

The patient returned to The Clinic in March, 1933. For about six months he had had a sensation of tightness and soreness in the thorax which had increased gradually and had been accompanied by a rather severe cough. He had not noticed any fever, but itching, pain in the lower part of the abdomen, and weakness and loss of weight were mentioned. The nasopharynx and pharynx were normal, but a roentgenographic examination, on March 7, disclosed "extensive metastasis to both lungs."

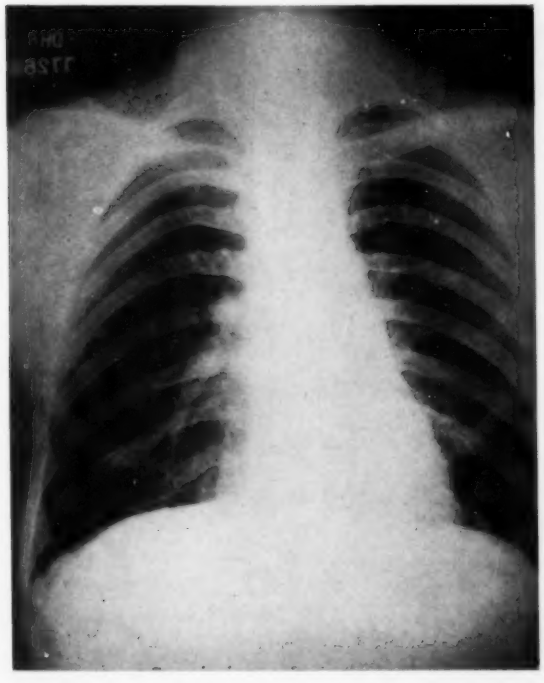

Fig. 5. Case III. Roentgenogram of the thorax June 9, 1931, showing persistent widening of the shadow cast by the mediastinal structures and slight residual enlargement of mediastinal nodes, especially at the hilus of the right lung.

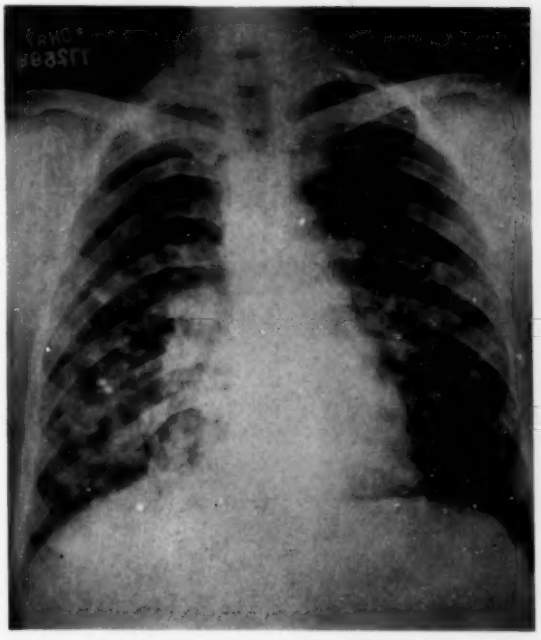

Fig. 6. Case III. Roentgenogram of the thorax March 7, 1933. Extensive nodular metastasis or infiltration throughout both lungs.

Inspection of the roentgenograms revealed innumerable nodules of different size scattered throughout both lungs (Fig. 6). These nodules seemed rather large for a tuberculous process, but the possibility could not be excluded. On the whole, however, the antecedent history and clinical manifestations and physical findings made a diffuse, nodular, lymphoblastomatous infiltration of the lungs most likely. To distinguish between these two possibilities, another course of roentgen treatment, directed mainly to the lungs but also to the cervical, axillary, inguinal, and lumbar regions, was given between March 8 and 11. This was followed by such rapid improvement that the idea of pulmonary tuberculosis had to be discarded in favor of lymphoblastomatous infiltration.

When the patient returned in September, 1933, his condition had improved considerably as far as the respiratory tract was concerned, but, during the preceding month, the cough seemed to increase again, and complaint of pain in the upper part of the abdomen was made. All the superficial lymph nodes were now reduced to barely palpable granules, but a sensation of deep resistance on palpating the upper part of the abdomen pointed to persistent enlargement of the retroperitoneal nodes. A roentgenogram of the thorax, made

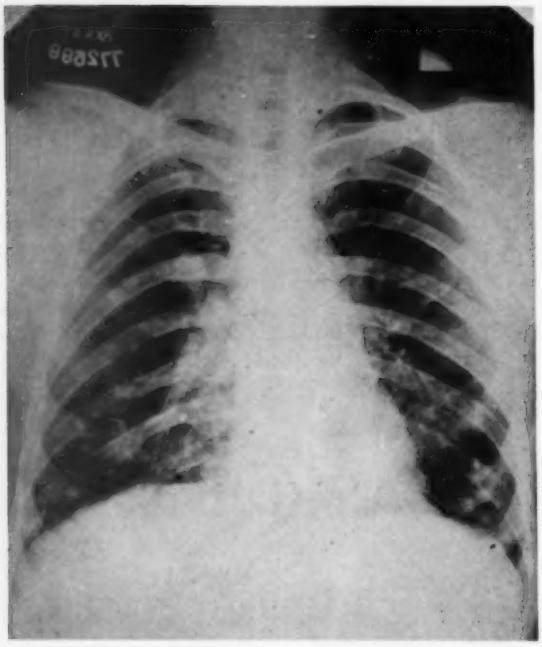

FIG. 7. Case III. Roentgenogram of the thorax September 12, 1933. Marked resolution of the nodular infiltration in both lungs.

on September 12, 1933, showed marked resolution of the greater part of the nodular, pulmonary infiltration (Fig. 7). Another course of treatment to the thorax and abdomen was given between September 12 and 16, 1933. In October the cough had greatly improved and the abdominal pain and general pruritus had disappeared. Comparison of a roentgenogram made on October 10, 1933, with the previous ones revealed still greater improvement in the condition of the lungs (Fig. 8).

This patient has not been seen since that time, but he was admitted to the University Hospital, Minneapolis, in April, 1935, and a roentgenogram made there and graciously forwarded by Dr. Rigler showed the condition of the lungs to be even better than it had been in September and October, 1933.

*Lymphoblastomatous Infiltration.* While uncommon, lymphoblastomatous infiltration of the lungs is not rare. Sometimes it is confined to the upper or to the central portion of the lungs, but sometimes, as in Case III, it may be rather widespread. Such nodular infiltration probably means lymphoblastomatous invasion of the small lymphoid nodules related to the bronchial tree. From a diagnostic point of view, the problem is to distinguish it from tuberculosis. The history and clinical features usually give invaluable assistance but, when lymphoblastoma is etiologically related to a tuberculous process, recognition of the character of the pulmonary lesions becomes clinically difficult. Here, radiotherapy may render invaluable service. If exposure of the lungs to a moderate quantitative dose of roentgen rays through four fields is followed by rapid improvement in the condition of the patient and by corresponding resolution of the infiltrative lesions, the conclusion that these were of the nature of lymphoblastoma is inescapable. It has long been well known that the response of tuberculous lesions to irradiation is characteristically slow and contrasts sharply with the rapid action of irradiation on lymphoblastomatous lesions.

CASE IV. The patient in this case was a man, aged forty-six, who registered at The Clinic on May 10, 1929. In July, 1928, severe abdominal cramps had suddenly developed and had continued for two or three days. This had not been

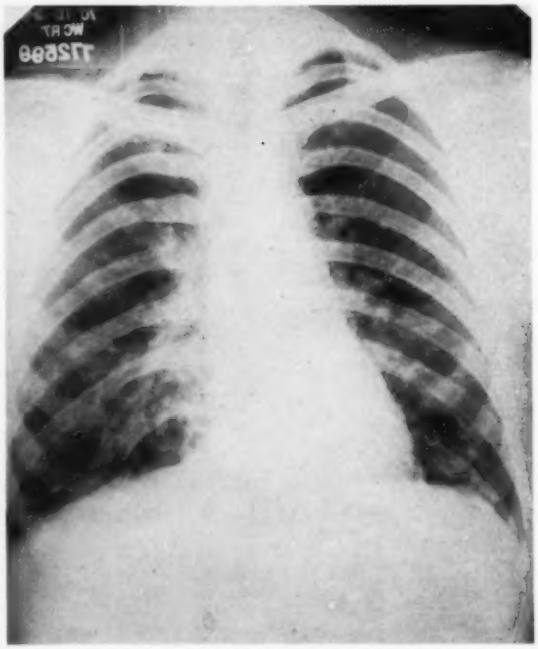

FIG. 8. Case III. Roentgenogram of the thorax October 10, 1933. Almost complete resolution of nodular infiltration in both lungs.

accompanied by nausea, vomiting, or diarrhea. For several days afterward the patient had been conscious of a heavy sensation in the epigastric region. About two weeks later, he had become aware of a slight daily fever which had been accompanied by lassitude and had continued about two weeks. He then had recovered his usual health until September 1, 1928, when he had a temperature of about 100° F. for ten days. On September 28 a third attack had begun, and this time the afternoon temperature had risen to 101° F. A fourth attack had started on October 20, 1928, and the temperature had mounted to 103° F. Each bout of fever had lasted about ten days. Between times he had felt quite well. On November 11, 1928, another attack had begun, and for about two weeks the temperature had varied between 102° and 105° F. During this bout the patient had been admitted to a hospital and had been said to have a positive Widal test. After the fever had subsided, he had been up and about for only five days when, on December 15, 1928, fever had recurred. He had returned home on January 1, 1929, free from fever, but on January 15 the temperature had again risen to 102° F. and the fever had lasted about twelve days. Typhoid vaccine had then been administered and, during the two weeks that he had been confined to bed, he had remained free from fever. But as soon as he had left the bed the fever had returned. Since then he had had similar attacks about once a month, each attack lasting from ten to fifteen days. At no time after the first attack had the fever been accompanied by pain or digestive disturbances, but he had little or no appetite and was weak. The bowels had always functioned regularly, except during bouts of fever.

Inability to eat during the periods of fever had caused him to lose weight, but he had recovered this soon after the fever disappeared. His weight was only 10 pounds (4.5 kg.) below the normal level. At one time, in December, 1928, he had become very weak and, although he regained some strength, he still remained rather weak. The latest bout of fever had been accompanied by cough. He had been free from cardiac or gastrointestinal disturbances since the initial attack, but during several attacks bleeding from the nasal mucous membrane had occurred. Prior to this illness he had had dental difficulties of an unrecorded nature and, in January, 1935, one tooth was said to have "ulcerated."

On examination, a number of moderately enlarged cervical, axillary, and inguinal nodes were found. A deep, boggy induration in the epigastric, left hypochondriac, and umbilical portions of the abdomen, with resistance and tenderness on palpation, pointed to enlarged retroperitoneal nodes as a part of the lymphoblastomatous process. A node, removed from the left axilla and examined microscopically, was reported as revealing lymphoblastoma of the Hodgkin's type. Between May 27 and June 5, 1929, a course of roentgen treatment was directed to the cervical and axillary regions as well as to the entire trunk, including the groins. This was done with rays generated at 135 kv. (peak), filtered through 4 mm. of aluminum (neck, axilla, anterior abdomen and groin), or through 6 mm. of aluminum (anterior and posterior thoracic, lower thoracic, and lumbar fields on each side), each field receiving approximately 600 r measured in air.

The fever and pruritus diminished rapidly and disappeared and the patient's strength increased. About the middle of June, edema of both ankles developed, probably from vascular obstruction by enlarged iliac nodes. A second course of treatment, similar to the first, was given between July 2 and 9, 1929. When the patient returned, at the end of July, his weight had increased 5 pounds (2.3. kg.), the edema of the ankles had disappeared, the fever and itching had not returned, and his general condition was excellent. A third course of roentgen irradiation was directed to the abdomen, through four anterior and four posterior fields, between July 30 and August 2, 1929.

In October, 1929, fever again developed, the patient's appetite and strength diminished perceptibly, and he became unduly slow in thought and speech. It seemed so obvious that the abdominal nodes were again active and that metastasis to the brain had taken place that, between October 16 and 23, a course of roentgen irradiation was directed to the upper two-thirds of the abdomen through two anterior and two posterior fields, and to the entire cerebrum through four fields; the conditions of irradiation were similar to those used on previous occasions. Within one week the manifestations of cerebral metastasis (marked slowness of thought and speech) disappeared. When the patient returned in November, his cerebral processes were entirely normal and the fever and itching had disappeared. Another course of treatment, directed to the head only, was

given on November 20 and 21, 1929. One week before Christmas, diarrhea and fever developed and continued for about ten days, after which they gradually subsided. On January 16 and 17, 1930, roentgen irradiation was directed to the upper two-thirds of the abdomen through two anterior and two posterior fields. A period of considerable improvement followed but, in March, 1930, the fever returned and the patient's strength gradually waned. He died on May 6, 1930.

This case is interesting chiefly because of the cerebral metastasis and its prompt disappearance after irradiation of the head, but it also illustrates another important point. The duration of the disease in different patients varies a great deal. While this may have some relation to the extent of involvement in many cases, in others the relation between the duration and extent of the disease is not nearly so obvious as one might expect. The most significant factors in the duration of the disease, and therefore in the probable survival of the patient are the relative acuteness or chronicity of the pathologic process and the thoroughness of treatment. When lymphoblastoma develops in children or young adults, its course tends to be more rapid than in older persons, in many of whom, especially those who have received systematic and thorough treatment, the disease may continue for years. In other words, periods of moderate lymphoblastomatous activity may be interrupted by long intervals during which the disease is in abeyance. During such periods of relative arrest, the patient may feel as well as ever and may be able to carry on all his usual activities and may even be able to do hard physical labor. It is not uncommon for such patients to survive for ten or fifteen years. In the majority of cases in which the disease is not acute, the degree of chronicity varies greatly.

*Infection.* An uncommon complication, examples of which cannot be cited for lack of space, is the association of infection and lymphoblastoma, not as an etiologic factor but as a part of the disease. To make our meaning clear, a patient may present himself with enlarged cervical nodes but, besides the hyperplastic nodes, there is evidence of acute infection of the cervical tissues, diffuse swelling and induration, redness of the overlying skin, tenderness, and fever, the character of which suggests a septic process. The reason for drawing attention to this complication is that it has a marked influence on the radiosensitiveness of the lymphoblastomatous nodes. Instead of undergoing rapid retrogression during and after irradiation, as may be expected when secondary infection is not present, the affected lymph nodes hardly change at all until an outlet for the pus has been provided by surgical means. Otherwise, surgical procedures may be hazardous. Once this has been done, the enlarged lymph nodes may usually be counted on to retrogress at the ordinary rate. In some cases, however, the lymphoblastomatous nodes do not recover their usual sensitiveness to irradiation for a short time. Unfortunately, secondary infection may not infrequently prove to be a sinister complication, and death may supervene because active measures to relieve the situation are not taken until it is too late.

### TECHNIQUE OF IRRADIATION

Concerning the technique of irradiation for lymphoblastoma, some divergence of opinion still exists. Impressed by the immediate recession of lymphadenopathy when the affected regions are exposed to rays generated at 200 kv. (peak), some physicians are not aware that equal or better results may be obtained with rays generated at 135 kv. (peak) and filtered through 4 mm. or 6 mm. of aluminum, according to the situation of the nodes. Since the disease tends to extend from one group of nodes to another, regardless of the technique of irradiation, and since permanent cure in all but very few cases is out of the question, the course of wisdom would seem to be to adopt a technique that can be repeated at intervals for an indefinite period. Treatment with rays generated at 200 kv.,

unless the quantitative dose per field is considerably below the limit of tolerance of the skin, may not be repeated more than a few times without risk of jeopardizing the integrity of normal tissues or of inducing deleterious changes in the cellular elements of the blood. When, on the other hand, full or tolerance doses of rays generated at moderate voltage are employed, the same or even greater danger must be faced. But when only a moderate quantitative dose of similar rays are directed to each field, the treatment may often be repeated at intervals for months or years without much loss of radiosensitiveness on the part of the diseased cells. Under these conditions, also, deleterious changes in the blood are less likely to occur. The greater penetration of rays generated at 200 kv. is a disadvantage. The lymphoid tissues are so radiosensitive that such penetration is unnecessary. In the long run, the interests of most patients suffering from this disease seem to be more effectively served when manifestations of the disease are treated with moderate doses of rays generated at moderate voltage.

Much more important than the voltage at which the rays are produced, however, is the precise method or plan of irradiation. By this is meant the number of beams of rays with relation to the clinical manifestations of the disease and to the physical findings, the care with which the beams of rays are directed to the affected regions, and the quantitative dose per field. Maximal doses are to be avoided because of the danger of inducing cutaneous changes which may shortly prevent subsequent treatment. Patients who have been subjected repeatedly to maximal doses may subsequently become pitiful examples of such excessive zeal.

DISCUSSION

Dr. Frank W. Konzelmann, Philadelphia. There has been a growing tendency in America in recent years to classify Hodgkin's disease among the lymphoblastomas. I think that this is dangerous, for we will soon be in the same state of confusion as we were a number of years ago when all cases of lymph node enlargement, without a leukemic blood picture, were called pseudoleukemia. Those who support the infectious nature of Hodgkin's disease have a great many points to support such a view. Personally, I support the neoplastic theory of Hodgkin's disease. Dr. Peirce and Dr. Jacox have well demonstrated the importance of the roentgen ray in the treatment of Hodgkin's disease. Dr. W. E. Chamberlain, at Temple University, has had a similar striking success in the treatment of cases.

Dr. Konzelmann then showed a few slides, and concluded by saying:

I was very interested in what Dr. Desjardins had to say about the relation of abdominal node enlargement to pruritus. We had not noticed such a relationship in our cases and it will be with a great deal of interest that I shall review my own autopsy material in the light of what he said.

I found these presentations not only very interesting but very instructive, for many new thoughts have been added to what I already know of Hodgkin's disease.

Dr. Peirce (closing). I wish to concur in Dr. Desjardins' comments regarding the clinical symptoms of lymph node involvement, although we did not enter into a widespread discussion of this point. Pruritus is common, particularly in those patients who have never had any irradiation over the abdominal nodes. That was true in the two cases of pleural involvement which I showed.

I appreciate very much Dr. Konzelmann's comment. We believe Hodgkin's disease belongs to the neoplastic group, but there are certain arguments which can be employed and are employed very legitimately in the consideration of a possible inflammatory inciting cause.

Dr. Desjardins (closing). I am grateful to Dr. Konzelmann for being so considerate. About abdominal involvement, until ten years ago I did not realize its significance, but gradually the relationship between abdominal involvement and the itching, the fever and cutaneous manifestations in many cases became so overwhelming that they could not be disregarded. Now, when a patient complains of itching, fever, with or without cutaneous manifestations, therapeutic attention is first concentrated on the abdomen, and in a short time the symptoms diminish and the patient's condition improves. It will be interesting to see if the experience of others will confirm our own.

# ORDERLY PROCEDURE IN THE ROENTGEN DIAGNOSIS OF INTRATHORACIC TUMORS

*By* WILLIAM H. STEWART, M.D., *and* H. EARL ILLICK, M.D.
NEW YORK CITY

ROENTGEN examination of the thorax too often is limited to roentgenoscopy and roentgenograms in the standard posteroanterior position. Too little effort is made to use certain well-known positions or procedures which may aid greatly in establishing the diagnosis.

In the case of neoplasms the patient may be examined a great many times during the course of the disease. These comparative re-examinations can be of added benefit if with the above ordinary technique is combined reasonable variation and orderly procedure so that the greatest possible diagnostic information may be obtained.

It is the purpose of this brief presentation to call attention to some of the less commonly used methods of roentgen examination of the thorax and attempt to suggest when they may be used to best advantage. These procedures may be enumerated and considered under the following headings:

1. Roentgenoscopy
2. Roentgenography
3. Pneumothorax with or without aspiration
4. Bronchography
5. Esophagraphy

1. *Roentgenoscopy*. The patient coming for diagnosis of a chest lesion is first given a preliminary roentgenoscopy in all possible positions. From the information thus obtained, a roentgenographic examination is made which will serve to bring out the salient diagnostic features.

The roentgenoscope used is shock-proof and permits instantaneous roentgenographic exposures at a predetermined setting, if desired. Thus if a lesion is well demonstrated at some unusual angle during roentgenoscopy, a roentgenogram may be made immediately to record the finding.

A motor-driven tilt-table is also available for the patient too sick to stand which permits positioning in any conceivable attitude.

2. *Roentgenography*. The usual stereoscopic posteroanterior films are routine but in addition other valuable postures may be indicated, such as:

(*a*) True Lateral: In this attitude the patient has the diseased side against the film, the roentgen tube opposite and the arms elevated above the head. A sagittal view of the thorax results. This is especially useful for outlining the position of the interlobar fissures and mediastinal relations.

(*b*) Lateral in the Prone Position with the Affected Side Uppermost: The film may be anterior or posterior; the tube opposite. The patient lies on the normal side, compressing the lung and forcing maximum expansion of the affected side. This will bring out the costophrenic angle region most satisfactorily, demonstrating the degree of areation. *Fluid levels are detected in patients too weak to stand.* When bedside examinations are made, this film is a necessity. It is most valuable in routine examination of post-pneumonic complications.

(*c*) Oblique: Erect or prone. Roentgenoscopically, the examiner may find that one or the other oblique position best demonstrates the lesion; this is especially true in mediastinal growths. A tumor causing only slight abnormality when viewed in ordinary stereoroentgenograms may be of considerable size when viewed obliquely. Films taken immediately on the roentgenoscope may best demonstrate these changes.

(*d*) Potter-Bucky Films: Very rapid chest examinations made without a Potter-Bucky at 1/30 second with low kilovoltage are used to bring out the finer pulmonary

detail necessary for the early detection of pulmonary tuberculosis but do not always penetrate densities due to tumor or inflammation. Such areas due to consolidation around abscess cavities, bronchiectasis, tumors and such lesions are poorly defined requiring better penetration and higher kilovoltage. In such cases a film made with the Potter-Bucky diaphragm, the patient erect or supine, may give valuable information such as fluid levels, bone erosion, calcific deposit in the tumor or pericardium or tumor masses behind the heart shadow.

3. *Pneumothorax with or without Aspiration.* The findings with the above methods may reveal only a dense shadow occupying a portion of the chest on the affected side, which may be due to free fluid in the pleural cavity or to tumor masses. If pleural exudate is present, it is important to withdraw as much as the patient can comfortably stand and replace with air. Fluid may need to be withdrawn daily for several times and air introduced. Pneumothorax is a method of extreme value in the recognition of malignancies of the lung, pleura and mediastinum.

4. *Bronchography.* This is the next important step in the diagnosis of tumors and

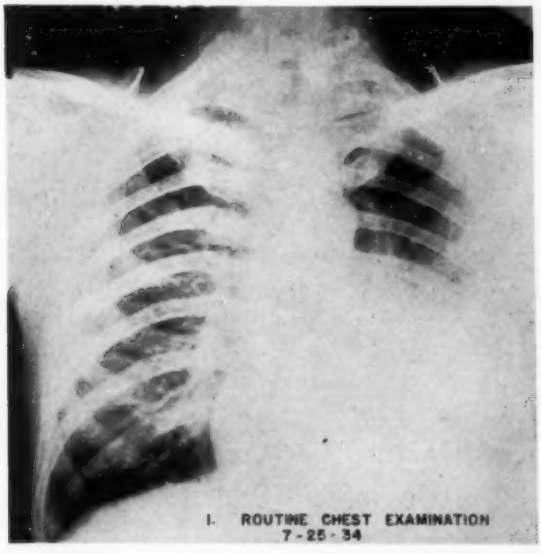


Fig. 1. July 25, 1934. An indefinite density at the left base. What is the lesion?

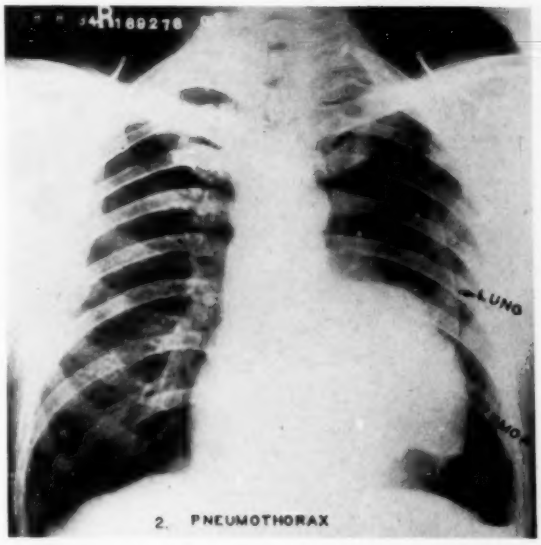


Fig. 2. August 8, 1934. Following pneumothorax the tumor mass is demonstrated in the lower lobe.

obstructions. We use any one of three methods to introduce the opaque oil.

(*a*) At the time the bronchoscopic examination is made, the opaque material can be injected through the bronchoscope directly into the diseased area which is recognizable by the condition of the mouth of the bronchus or the detection of pus exuding. This procedure is carried out under roentgenoscopic control on a machine with a switch-over arrangement so that at any time a film may be made by increasing the current.

(*b*) The second technique is *bronchography by the drop method;* it is one commonly used. In skilled hands excellent results are obtained. The dependence upon posture, however, may interfere with an extensive roentgenoscopic study. The entire roentgenoscopic and roentgenographic study must be done rapidly. Coughing or slight change of posture may render the examination unsatisfactory.

(*c*) The third method, and the one preferred by our Roentgen Department, is easily performed after a little practice. A catheter is passed into the trachea after preliminary local anesthesia and under the roentgenoscope, the tip of the catheter is placed in the best possible relation to the

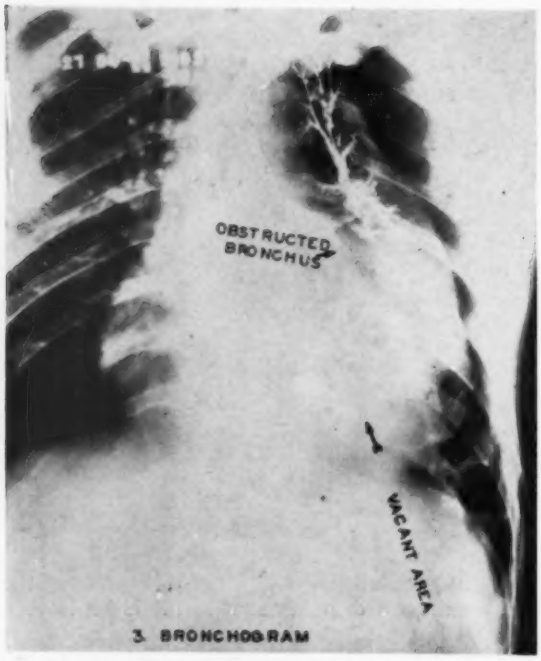


Fig. 3. August 27, 1934. A bronchogram reveals obstruction to the left lower main bronchus from primary intrabronchial invasion of the tumor.

bronchi to be filled. The patient is correctly postured so that the involved bronchi may be filled by the oil. The opaque material is then injected as found necessary by roentgenoscopic study and the peripheral bronchi can be studied as well as the main bronchi. Stereoroentgenograms are exposed as indicated to record the findings.

Any standard method is satisfactory; the success depends on the skill of the operator with his own particular technique more than the method employed. Bronchograms are best made with the Potter-Bucky diaphragm, which brings out dilated bronchi and obstructive lesions very satisfactorily. Such study delineates the exact site and character of the disease process and are indispensable when thoracic malignancy is suspected.

5. *Esophagraphy*. Finally, one can beautifully outline a tumor, especially of mediastinal origin, by introducing opaque material into the esophagus. The esophageal displacement may give most gratifying information to the surgeon.

Figures 1, 2, 3 and 4, all of the same patient, demonstrate the value of some of these methods.

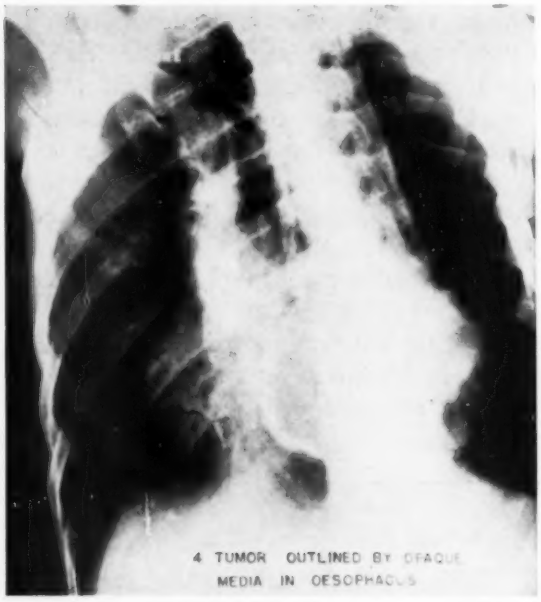


Fig. 4. October 13, 1934. The esophagus filled by barium outlines the mediastinal bulk of glandular metastases.

VOL. 36, NO. 2

# RIGHT-SIDED AORTA

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RIGHT-SIDED aorta due to persistence of the right fourth branchial arch is a rare anomaly, but is of importance to the roentgenologist since the ante-mortem diagnosis rests entirely upon the roentgen examination. Most cases are asymptomatic, but the anomaly may be a cause for dysphagia (the so-called dysphagia lusoria), dyspnea, cyanosis, hoarseness, cough, pain in the chest, vomiting, palpitation, and indefinite sensations in the arms as pointed out by Sprague, Ernlund and Albright. We have recently observed 2 cases which were sent to cancer clinics for radiation therapy with the erroneous diagnosis of mediastinal tumor, probably Hodgkin's disease. In the third case reported here, the anomaly produced slight dysphagia, but was not the presenting symptom. The patient had been examined several times for duodenal ulcer before the anatomical variation of the aorta was discovered.

The first description of a living case of right-sided aorta, later confirmed by autopsy, was published in 1913 by Mohr. The ante-mortem diagnosis was based on the roentgen studies of Albracht and Assmann. The roentgen picture is further described by Assmann in 1924. Arkin reviewed the literature in 1926, and reported 2 cases. In the same year, Renander reported one case which was the first living case described in the English literature. Blackford, Davenport, and Bayley reported one case in 1932 which was associated with another anomaly of the great vessels.

Biedermann found 12 specimens of right-sided aorta in the Pathological Institute of the University of Leipzig. Eight of these specimens were found between 1904 and 1919, during which time about 20,000 autopsies were performed in the Institute. This means that there was one case of right-sided aorta in every 2,500 post-mortem examinations. Of these 12 cases, 6 showed other congenital anomalies of the heart or great vessels, but in the remaining 6 cases the right-sided aorta was the only anomaly. Biedermann, in a period of fifteen months, during which time roentgen examination was made of 5,000 chests, discovered 7 cases of right-sided aorta. The anomaly gave no symptoms in those 7 cases and was an incidental finding.

## EMBRYOLOGY

The embryological development of the great blood vessels, as given by Jordan and Kindred, is shown in Figure 1. The

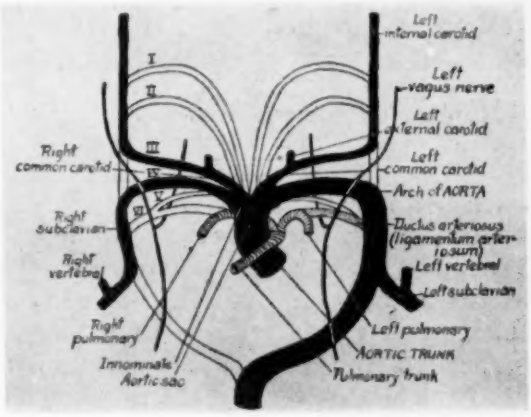


FIG. 1. Diagram illustrating the transformation of the aortic arches (Jordan and Kindred).

transformation of the six paired branchial arches is depicted diagrammatically. Normally the fourth branchial arch on the left develops to form the base of the systemic aorta. The portion of the right dorsal aorta between the subclavian and common dorsal aorta disappears and the remainder of the fourth arch forms the base of the subclavian artery on the right.

In the anomaly of right-sided aorta this development is reversed. The left fourth branchial arch is obliterated with the exception of a small diverticulum-like sac corresponding to the distal portion of the arch, 1.5 cm. to 3.5 cm. in length, from

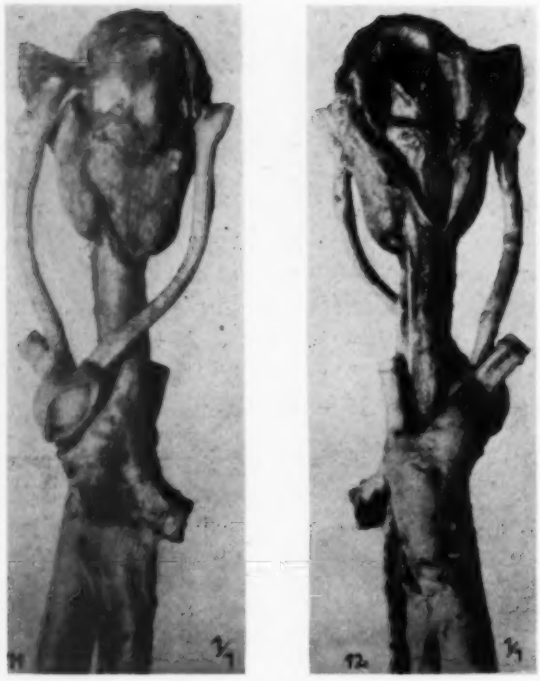

Fig. 2. Anterior and posterior views of a specimen of a right-sided aorta (Biedermann).

which arises the left subclavian artery. The communication between the right fourth branchial arch and the common dorsal aorta persists, thus forming the right-sided arch which displaces the trachea and esophagus to the left. The diverticulum-like protrusion (which normally would have become the left-sided aorta) lies behind the trachea and esophagus. The amount of displacement of the trachea and esophagus depends largely upon the size of the diverticulum. These relationships are clearly seen in Figure 2 which is a reproduction of the specimen of Case 11 from Biedermann.

## CASE REPORTS

Case 1 (P. M. H. 4193). White female, aged seventy-four, was referred to the Hospital with a diagnosis of mediastinal tumor. During routine examination of the gastrointestinal tract made elsewhere, a mass was discovered in the upper posterior mediastinum which was diagnosed as probable Hodgkin's disease and the patient was referred for high voltage roentgen treatment. On questioning, the patient recalled that she had had slight difficulty in swallowing solid food ever since an attack of laryngitis one year previously. She had paid little attention to this. Physical examination was essentially negative.

The roentgen examination of the chest, in the anteroposterior view, shows the mediastinal shadow to be essentially normal in appearance except that the trachea is slightly displaced to the left (Fig. 3). This alone would probably not be thought significant. There appear to be aortic knobs on both sides, both showing calcium deposited in their periphery (Figs. 3 and 4). In the right or first oblique view, the trachea is seen displaced forward at the level of the aortic arch. There is a mass posterior to the trachea which obscures the posterior mediastinum at this level. One then observes that in the oblique position the normal aortic arch is not visible.

With the esophagus outlined by a barium meal, the characteristic deviation from its normal course is seen. Beginning at the level of the inner margin of the left clavicle, the esophagus describes an arc to the left and returns to its normal position at the level of the 7th thoracic vertebra. In the right or first oblique position the esophagus is displaced forward and follows the course of the displaced trachea (Fig. 5). There is narrowing of the

Fig. 3. Case 1. Anterior view without barium in the esophagus. No noticeable abnormality.

Fig. 4. Case 1. Esophagus outlined with barium. Note the characteristic narrowing and displacement to the left. There is calcium deposit in the diverticulum and also in the right-sided aortic arch.

Fig. 5. Case 1. Right oblique view. The esophagus is displaced anteriorly and narrowed. The trachea is likewise displaced anteriorly. The usual shadow of the aortic arch is absent.

Fig. 6. Case 1. Left oblique view. The space between the ascending and descending portion of the aorta is narrowed. The aortic diverticulum with calcium in its periphery is shown behind the esophagus.

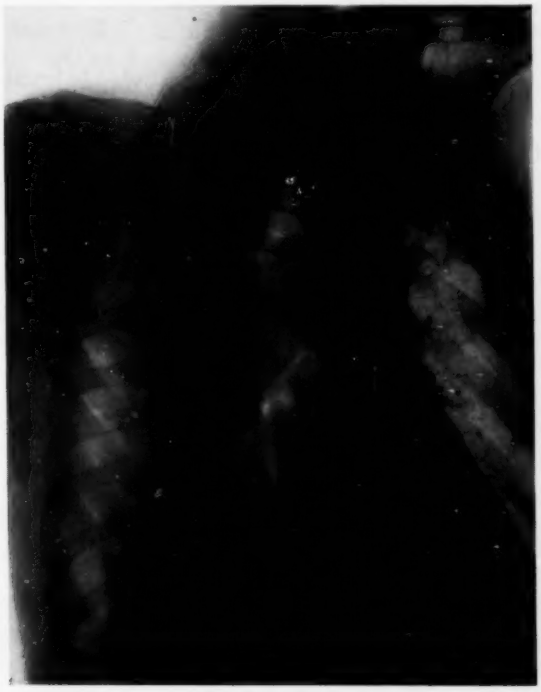

Fig. 7*a*. Case 11. Right oblique view without barium in the esophagus. The aortic diverticulum obscures the upper posterior mediastinum and displaces the trachea anteriorly.

Fig. 7*b*. Case II. With barium in the esophagus, the characteristic displacement and narrowing are seen.

esophagus in both the anteroposterior and oblique views. In the left or second oblique position the displacement and narrowing of the esophagus are also seen (Fig. 6). The space between the ascending and descending aorta is much narrowed. The mass in the upper mediastinum lying behind the esophagus is seen to pulsate and there is calcium in its periphery.

Case II (P. S. H. 7753). White male, aged seventy-one, was admitted to the Pondville Hospital at Norfolk (Massachusetts State Cancer Hospital). He had been seen at another institution three weeks previously, at which time a diagnosis of coronary occlusion was made. Roentgen examination of the chest had shown a mass in the upper mediastinum which was thought to be Hodgkin's disease and the patient was sent to the Pondville Hospital for radiation therapy.

The chest presented essentially the same roentgen picture as that described in Case I. The anteroposterior view showed slight displacement of the trachea to the left and slight prominence of the mediastinal shadow to the right at the level of the aortic arch. In the oblique views there was a mass in the upper posterior mediastinum displacing the trachea forward (Fig. 7). A barium meal showed the esophagus also displaced to the left and anteriorly.

Case III (M. G. H. 11697). White female, aged forty-five, examined at the Massachusetts General Hospital by Dr. G. W. Holmes, to whom we are indebted for the privilege of reporting this case. The patient complained of epigastric pain for which she had been examined several times previously with negative findings. Dr. Holmes demonstrated the presence of a duodenal ulcer and in addition discovered a right-sided aorta. On further questioning the patient, it was found that she had had slight difficulty in swallowing.

A film of the chest appeared normal in the anteroposterior view but on filling the esophagus with barium the characteristic displacement to the left and anteriorly was shown (Fig. 8).

## DISCUSSION

Three cases of right-sided aorta are reported. In 2 cases there were symptoms of slight dysphagia and in 2 cases an erroneous diagnosis of mediastinal tumor had been made by roentgen examination and the patient referred to cancer centers for

Fig. 8. Case III. Anterior view. The barium-filled esophagus is displaced to the left and narrowed.

radiation therapy of what was supposedly Hodgkin's disease.

The examination of the esophagus is of paramount importance in making the diagnosis. In the anteroposterior view the esophagus is displaced to the left at the level of the clavicle and in the oblique and lateral views it is displaced anteriorly. There is narrowing of the esophagus in all views. The trachea is also displaced forward and to the left. There is a prominence in the region of the aortic arch on the left which simulates the true aortic knob, but which is in reality a diverticulum-like vestige of the left aortic root. This diverticulum varies in size, thus causing some variation in the displacement and narrowing of the esophagus and trachea. One of the cases reported showed calcification in both the right-sided arch and in the vestige of the aortic arch on the left side. This calcification which has hitherto not been reported in a case of right-sided aorta outlines clearly the anatomical variation. The fact that this condition may be confused with a mediastinal neoplasm makes it important that the roentgenologist should be familiar with this characteristic picture.

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# MARCH FOOT

*By* JOSEPH F. ELWARD, M.D.
WASHINGTON, D. C.

THE affection of the metatarsal bones which is manifested by painful swelling of the forefoot, with concomitant spontaneous fracture of one or more of these bones, called generally in English "march foot," presumably because of its supposed association with military activities exclusively, has been variously, and probably more or less inaccurately, entitled by European investigators "Deutschländer's disease," "Marschgeschwulst," "Fussgeschwulst," "Marschfraktur" in Germany; "fracture de marche," "fracture de recrue," "pied debile," "pied forcé," "pied de marche," "l'enflure du pied," and "pied surchargé" in France. However, results of more recent researches into the etiology and pathogenesis of the disease in question appear to point to "pied forcé" (forced foot) and "pied surchargé" (overloaded foot) as designations of choice, the first for the acute form, as it is observed in athletes, soldiers, and all who are subjected to sudden and unaccustomed overexertion, and the second for the chronic form, as noted in clerks, domestics, and those who are required to stand for long periods without adequate intervals of rest.

Although Deutschländer is almost universally credited with the original observation and description of the disease which bears his name, the first actual reference to the condition in medical literature was made by Breithaupt, who in 1855 reported the occurrence of persistently painful and edematous feet in soldiers following long forced marches, the affection having been diagnosed and designated by him as traumatic inflammation of the tendon sheaths. Breithaupt himself suffered from the disability and recorded in considerable detail his own symptoms as well as those of civilian and military patients under his care. In 1877, Weisbach described an affection of the feet of infantrymen which usually supervened quite suddenly on the second or third day of forced marching and was believed to be due to traumatic (lacerative) inflammation of the intermetatarsal ligaments. This condition Weisbach called "syndesmitis metatarsea," and he proposed the substitution of this term for the older and less accurate designations of "swelling of the foot," "oedema pedis," etc., by which the affection had previously been known.

Ten years later, Pauzat published the results of clinical observations of 8 cases of osteoplastic periostitis of the metatarsal bones from overexertion during protracted marches, occurring in conjunction with the edematous condition of the feet originally described by Breithaupt and caused apparently by direct traumatism resulting from pressure by the dorsal fold of the shoe, without alteration of superficial tissues at this point. In 1888, Poulet from a study of 11 cases of the disability described by Pauzat which had come under his observation, assumed an underlying cause of rheumatic osteoperiostitis, regarding the latter as merely a manifestation of the rheumatic diathesis localized in the foot, inasmuch as that organ functioned more than the rest of the organism and became more fatigued during military marches. Martin in 1891, from the observation of a series of 18 cases of his own, arrived at the conclusion that the condition described by Pauzat and Poulet resulted from synovitis and arthritis of the joints of the forefoot, induced by weakness of the plantar ligaments and compression of the forefoot between the ground and the weight of the body.

In 1897, Busquet reviewed the investigations of his predecessors from Breithaupt to Martin, and described under the title of ossifying periostitis of the metatarsals a condition similar to the one previously observed by them, dividing cases of the particular form of periostitis in ques-

tion into two etiological groups, namely, traumatic and diathetic. Schulte in the same year first recognized and described in detail the fracture involved in the condition, and called attention to the fact that the term "Fussgeschwulst" should replace the less accurate designation "Marschgeschwulst," since the disability was not associated exclusively with marching. In 1897 also, Stechow reported 3 cases of what he called "chronic edema of the feet" in which the diagnosis was established by means of the roentgen ray. Stechow was first to assign fracture of the metatarsals as the cause of swollen feet of soldiers. Boisson and Chapotot in 1899 contributed 6 cases of "pied forcé" to the literature, and ascribed its occurrence either to fractures of the diaphysis of the metatarsals or to arthritis and violent strain upon metatarsal articulations. In that same year, Thiele reported the results of the study of 17 cases encountered within a period of three and a half months, all in a single battalion, in 15 of which the diagnosis was confirmed by roentgen examination. Thiele asserted it as his belief that fractures of metatarsal bones by indirect force were more frequent than was generally assumed, and assigned fracture or at least infraction of the metatarsals as the cause of so-called "Fussgeschwulst."

Momburg, in 1904, attributed the condition to prolonged flexion of the metatarsals with consequent inflammatory reaction followed subsequently by fracture. From an exhaustive study of etiological factors previously adduced, Kirchner concluded in 1905 that all so-called "march feet" were due to fracture of the metatarsal shaft, with slight displacement owing to immobilization of fragments by surrounding structures.

In 1913 Bähr published the results of a thorough investigation of the mechanics of fractures involved in the occurrence of the condition in soldiers, with particular reference to its relations to the extent of development of the anterior frontal arch.

Eight years later, in 1921, Deutschländer described a peculiar disease of the metatarsals with abrupt onset of pain in the latter, in the absence of demonstrable trauma, as observed in 6 civilian females, involving an inflammatory affection of the second or third metatarsals, resulting, in his opinion, from bacterial invasion. According to Deutschländer, at first the roentgenogram revealed no change in the bone, but after six to eight weeks there was observed in all his cases an encircling periosteal new growth of bone, which, after persisting for some time, gradually became increasingly fusiform and less voluminous coincidently with disappearance of symptoms. Since 3 of his patients ran a low febrile course, and the callus appeared only after eight to nine weeks (instead of the usual three to four weeks in the case of fracture callus) and in view of the absence of a history of trauma, Deutschländer assumed that there was involved in all his cases a low grade hematogenous bacterial periostitis.

The etiological hypothesis thus formulated and proposed by Deutschländer immediately encountered opposition from all sides. The concept of an inflammatory origin was generally rejected, the so-called Deutschländer pathological picture being included by the majority of investigators of the subject with fractures or infractions of the metatarsal bones resulting from trauma. Nast-Kolb had previously assumed that there was involved a special process of ossification such as might occur after several weeks at the site of injury resulting from more or less severe trauma. Turner advanced a trophoneurotic theory of origin. Bittrolff, and Müller in particular, who by resection of a portion of the radius subjected the ulna to an abnormal mechanical demand, and observed a fusiform callus formation in the ulna opposite the radial defect without the slightest indication of fracture, regarded the changes in the ulna as the reaction of the bone to an abnormal mechanical demand as in the case of Looser's zones of transformation, the callus formation occurring not as the

result of a single trauma but in consequence of continual mechanical overdemand. Honigmann remarked upon the similarity revealed by so-called spontaneous fractures in bone pathology due to starvation, which represent not actual fractures but transformation zones of bone, and expressed the opinion that Deutschländer's disease belonged in this category. Blencke assigned as an etiological factor the vertical position of the metatarsals in a shoe with a high heel (slight infraction resulting from excessive flexion).

Jansen presented a new theory for the actual causation of the condition, stating his belief that march foot was due to overfatigue in weak feet, this overfatigue resulting in spasm of the interosseous muscles, which in turn caused stasis of blood and lymph in the tissues of the feet, with consequent swelling of the soft parts, and brittleness of bone tissue, leading eventually to fracture.

Greifenstein in 1928 emphasized the necessity for clear differentiation of infractions and fractures of the metatarsals from the pathological picture presented by Deutschländer's disease, and enumerated among possible etiological factors of the latter more or less marked modification in the statico-mechanical demand upon the metatarsus and (probably the most important of all) the functional capacity of bone. Greifenstein insisted that there was no foundation for the theory of an inflammatory origin of the disease, and asserted that the principal characteristic of the disease of the locally altered metatarsals consisted in a secondary infraction or fracture, with possible slight dislocation.

In 1931 Närvi reported his observations on so-called "march fracture" or Deutschländer's disease of the metatarsals and a similar disease of the tibia (Ollonqvist's disease), declaring himself of the opinion that in both diseases surcharge and overexertion provoke stasis and thrombosis of the soft parts surrounding the bone, entailing impaired nutrition in the periosteum, the chief source of nutrition of bone, while circulatory disturbances in the periosteum produce the swelling and tumescence observable clinically as a painful tumor on the dorsum of the foot and the tibia respectively. Närvi explained that during the progress of the disease resorption of bone develops in consequence of imperfect nutrition of the bone, visible in the roentgenogram as one or several light fissures, with subsequent appearance of callus formation and induration of bone. Närvi contested the theory of the infectious origin of Deutschländer's and Ollonqvist's disease and the possibility of their occurrence as the result of simple mechanical infraction due to excessive flexion.

Speed and Blake state that clinically the cases of "march foot" may be divided into two groups: the first group, in which there is no tumor formation or roentgen evidence of bone pathology, and in which the pain and swelling subside in seven to ten days and the foot returns to normal; the second group, in which the duration of symptoms is much prolonged. The onset is identical with the first group, callus formation is excessive, and if the case is seen early, and weekly roentgenograms are made, a fracture line is usually, but not always, seen. The average duration of symptoms in this group is three months.

In a very recent communication on the subject of pied forcé, or Deutschländer's disease, Zeitlin and Odessky conclude that the disease results from overloading of a foot weakened functionally and anatomically. In their opinion, of all the theories thus far advanced, namely, inflammatory, traumatic, neurogenic, and functional insufficiency, the latter merits chief consideration.

Since the roentgen picture of the affection in question, on which the diagnosis is almost entirely based, is already familiar to the majority of roentgenologists, in consequence of the large number of contributions to the subject which have appeared within the last decade, its description need not detain us here. In this connection our principal concern should be

with the imperative necessity for careful differential diagnosis between (*a*) sarcoma of the bone, (*b*) Köhler's disease, and (*c*) other pathological and traumatic conditions. Of these, the differential diagnosis from sarcoma is by far the most vital. For example, Dodd not long ago reported a case in which owing to an erroneous diagnosis of sarcoma a patient with Deutschländer's disease submitted to an amputation of the foot, while in one of Straus's cases excision of the metatarsal was performed for the purpose of verifying a doubtful diagnosis. Other similar instances could doubtless be cited. In view of the customary absence of a history of trauma, the presence of a sarcoma may very readily be assumed, but closer study of the roentgenogram fails to reveal the so-called fan-like sun-ray structure generally regarded as pathognomonic of osteogenic sarcoma, although according to Kolodny a similar arrangement is known to occur in other skeletal lesions, for example, chronic inflammatory processes. Serial studies at weekly intervals usually serve to reveal the true nature of the affection. The latter should likewise be differentiated from Köhler's disease, which attacks the distal ends of the metatarsals, as well as from alterations in epiphyseal zones resulting from late rachitic changes, syphilitic diseases of bone, all other types of fractures, and incipient flat foot.

Conservative treatment is indicated in the great majority of cases of the disease. Rest in bed, baking, baths, massage, and occasionally exercises designed to restore tone of exhausted muscles of feet and legs have all proved highly efficacious as therapeutic measures. Deutschländer himself obtained excellent results from the employment of passive hyperemia. Antiphlogistic therapy has also been applied with benefit to patients.

The following are the reports of 2 cases which have come under my observation:

### CASE REPORTS

Case I. J. D., white male, single, aged thirty-eight; said to be a "shell-shocked" veteran; no occupation; formerly a laborer. His past and family history are irrelevant. Present illness dates from about two weeks prior to first examination on April 27, 1933, when he first noticed some pain and swelling in the left foot, and was unable to continue work in the family vegetable patch. He attributes the condition of his foot to the use of a spading fork. Roentgen examination (April 27, 1933) shows a "feathery" deposit of bone on either side of the second metatarsal. A fracture line is not seen. The nature of the bone deposit is not exactly determined, but osteogenic sarcoma must be ruled out.

Examination on May 8, 1933, shows considerably more callus. A fracture line is not as yet apparent.

May 15, 1933: The callus is now more intimately associated with the metatarsal shaft. No fracture line. No destruction. The patient was now transferred to Walter Reed General Hospital.

July 12, 1933: Through the courtesy of Major John J. Moore, Walter Reed General Hospital, I am able to present the study made on this date. This shows some absorption of excess callus, and the metatarsal shaft is approaching the normal. The symptoms are subsiding. No fracture line is seen.

October 26, 1933: The metatarsal is normal except for slight thickening at the site of the supposed fracture; no fracture line apparent; no symptoms.

January 17, 1934: The metatarsal shaft is now almost normal except for slight thickening, and the patient is free from symptoms.

Case II. R. D. O., white, female, aged fifty-nine; weight 200 pounds. Occupation: Conducts rooming and boarding house. The past and family history are irrelevant. The present illness began four weeks prior to first roentgen examination October 22, 1934. The patient had worn for a few hours only shoes with a higher heel than usual. One week following this episode of high-heeled shoes, pain was noted in the left instep. After a week of discomfort a physician was called. No history of direct trauma could be obtained, and infection was suspected. Treatment was instituted with infection as the working diagnosis. After three weeks of ineffectual therapy the patient was referred for roentgen study. Roentgen examination of the left foot shows fracture of the shaft of the second metatarsal. The fragments are end to

end with slight lateral displacement. The alignment and position are considered to be quite satisfactory.

In view of the history of no direct trauma, this is in all probability a case of spontaneous fracture (march foot). No callus is noted.

The foot was immobilized in a plaster boot. After six weeks the patient was free of symptoms.

Roentgen study October 31, 1935, shows old solidly united fracture of the shaft of the second metatarsal. There is only slight thickening at the site of fracture.

### COMMENT

The first case is believed to be the acute form, because of the history of onset following sudden and unaccustomed strain in using a spading fork. This type is properly called forced foot (pied forcé).

The second case represents the chronic form wherein the symptoms are not definitely dated, but apparently follow prolonged strain as must necessarily ensue in a patient of excessive weight (200 pounds in this case) who follows an occupation requiring standing for prolonged periods. The episode of high-heeled shoes is possibly a factor, but probably a minor one. This type is properly termed overloaded foot (pied surchargé).

While no competent roentgenologist will make the mistake of diagnosing sarcoma in cases of march foot, it must be borne in mind that the similarity between new bone formation (callus) and osteogenic sarcoma is at times striking and the pathologist with a stained section before him may be in doubt. The points of differentiation between these two conditions may be stated as follows: In new bone of the normal reactive type the osteoblasts are relatively small, equal in size, and are associated with preceding connective tissue containing many spindle cells and fibroblasts, and are arranged in orderly rows about definite spicules of new bone. The histology of sarcoma shows a proliferation of connective tissue passing through the stages of spindle cells, osteoblasts, osteoid tissue, and new bone. Osteoblasts predominate, these having large deep-staining nuclei and a cytoplasm pointed in one direction like the tail of a tadpole. Among these cells a deep-staining osteoid substance is found. This direct ossification differs in these sarcomas from benign reactive bone seen in inflammatory conditions and osteitis fibrosa in two outstanding respects: first, the osteoblasts predominate and great numbers are packed in among the osteoid tissue in a disorderly fashion; the osteoblasts vary in size, giving rise to numerous large binucleated forms, and they are not lined in orderly rows about definitely formed true spicules; and second, the osteoid tissue is laid down helter skelter and bears no constant relationship to the amount of fibrous tissue or osteoblasts present. In some sections this osteoid substance may infiltrate everywhere, compressing the masses of osteoblasts between it. In other sections, the osteoid tissue may be relatively sparse and the osteoblasts and their precursors, the fibroblasts, may predominate, the osteoid substance being present only in scattered areas.

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# ANEURYSM OF THE ABDOMINAL AORTA*

## CASE REPORT

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THE literature indicates that aneurysm of the abdominal aorta is not common[1]. In 10,360 autopsies Müller[2] found 6 cases. Among 468 cases of aneurysm at St. Bartholomew's Hospital only 23 were abdominal.[2] Out of 81,338 patients at Bellevue Hospital only 3 suffered from aneurysm of the abdominal aorta,[2] and during a period of twenty-five years only 21 cases of aneurysm of the abdominal aorta were seen at the Presbyterian Hospital.[2]

The diagnosis of this condition is important not only to save unnecessary laminectomies but also to differentiate it from other abdominal conditions. After running a short course these aneurysms rupture into the viscera[3,4] or erode the vertebrae with the production of paraplegia and involvement of other organs.[4] Gregory[5] has shown that compression of the spinal cord has had little attention in aneurysm of the abdominal aorta and that it is often mistaken for spinal cord tumor, the diagnosis being made during laminectomy.

FIG. 1. The outline of the aneurysm is seen extending from the tenth to the twelfth dorsal vertebra.

The following case shows the importance of roentgenography in the diagnosis of these cases, not only because the diagnosis would not have been made otherwise but that laminectomy might have been attempted or the patient would have been encouraged to walk about during the period of improvement thus exposing her to the danger of rupture of the aneurysm.

B. C., a colored woman, aged forty, was admitted to Bellevue Hospital in February, 1934, complaining of paralysis of both lower extremities of three weeks' duration, and marked constipation. She claimed that prior to the onset of the paralysis she experienced weakness in the lower extremities for about a month. At this time she noticed a lump in her back. In January, 1934, her right foot became paralyzed and a little later she was unable to move her right leg. Three weeks later paralysis set in in her left foot and after admission to the hospital there was no motion in her left leg.

Her past personal history was negative except for a salpingectomy one year before admission. During her stay at Bellevue nothing was noted in the other systems except a systolic murmur at the apex, and the neurological examination showed no pathological reflexes or sensory changes, and the knee and ankle jerks were active and equal. The roentgen examination at that time showed considerable destruction of the bodies of the eleventh and twelfth vertebrae suggesting a neoplasm.

On March 5, 1934, the patient was transferred to the Neurological Service of the City Hospital. Neurological examination showed no coordinative, sensory, motor or reflex changes in the upper extremities. In the lower extremities there were paralysis and absent tendon reflexes. There was a positive Babinski toe

* From the Neurological Service of the City Hospital through the courtesy of Dr. George J. Plehn, Director of Radiology.

sign in the left foot and a positive plantar skin reflex.[6] The cranial nerves presented nothing positive except the pupils which were fixed to light but responded to accommodation. The sensory examination disclosed an absence of position and vibration sense in the lower extremities with a preservation of tactile pain and temperature perception. The upper abdominals were present and the lower absent.

The patient was sent to the radiological department from which Dr. Plehn submitted the following report:

The lower dorsal and upper lumbar region indicates a marked destructive lesion probably secondary to aneurysm. There is a complete destruction of the eleventh and twelfth dorsal, lower end of tenth and upper end of first lumbar vertebrae (see Figs. 1 and 2). The large shadow in the descending portion of the aorta is very suggestive of aneurysm (Fig. 1). The location is probably below the descending portion of the thoracic aorta as it enters the diaphragm.

Fig. 2. The destruction of the bodies of the eleventh and twelfth dorsal vertebrae is seen.

Fig. 3. Roentgenogram showing the interception of the lipiodol in its descent at the level of the eleventh dorsal vertebra.

On March 9 lipiodol was injected by the cisternal route and it was seen to stop at the level of the eleventh dorsal vertebrae (Fig. 3). On March 29 a pneumoperitoneum was done but it did not aid the better visualization of the aneurysm. The intravenous pyelogram showed the kidneys in their normal position. The roentgen examinations were repeated during the following month and showed some calcification of the mass.

The blood Wassermann was negative while the Kahn was 4 plus. Spinal fluid examination showed a 4+ Wassermann reaction and gold curve of 4443321000. The non-protein nitrogen was 26 mg. and the blood sugar 72 mg. per 100 c.c. The temperature ranged between 98° and 101° F., the pulse between 88 and 125 and the respiration was normal.

The patient was started on silver salvarsan and after one injection developed a Herxheimer reaction. Courses of bismuth and mercury were than instituted.

Further observation during the following

two months disclosed the tendon reflexes of the lower extremities becoming lively starting with the leg which showed a positive patellar jerk, positive Babinski and heel tap.[7] Vibratory and position senses remained absent, while tactile and temperature perception, occasionally questionably involved, remained unaffected after repeated testing.

The patient was observed for a period of one and a half years and during this intervalshowed variation in motor activity but little change in the sensory fields. The last roentgen examination disclosed no change after an extensive course of antiluetic therapy in the wards of Dr. A. B. Cannon. The last neurological examination showed a paralysis of both lower extremities, a bilateral patellar clonus, absent Achilles and plantar tendon reflexes with a preservation of the dorsal tendon reflexes of the foot.[8] The vibratory and tactile sensibility were hardly involved. The sensory picture associated with the paralysis and reflex changes forms a unique syndrome of anteroposterior compression of the cord, showing a sparing of the lateral columns with slight evidences of pressure upon the pyramidal tracts. Percussion in the area of involvement disclosed a dullness instead of flatness. Auscultation revealed a peculiar gurgling sensation and a distant bruit which were not heard in other portions in the area of the spinal column.

SUMMARY

1. A case of aneurysm of the abdominal aorta with erosion of vertebrae is presented.

2. Early roentgen diagnosis was helpful in preventing the subjection of the patient to a laminectomy, and influenced therapy that arrested the progress of the condition for one and a half years.

3. A syndrome of anteroposterior compression of the spinal cord was noted in this case.

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# INTRAHEPATIC STONES AND STONE FORMATION

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THE term of "intrahepatic stones" designates the *presence* and the *location* of the stones in the intrahepatic passages, regardless of the primary place of formation or origin of the stones. In contradistinction to this term we would designate with "intrahepatic stone formation" or "intrahepatic lithiasis" *processes* of primary stone formation within the intrahepatic passages, i.e., the hepatic duct, its secondary branches and the radicles. This differentiation seems to us to be based on well-established principles, not clearly postulated in the earlier publications. The former condition is by far the more common one, and most of the cases reported in the literature belong to this group.

Our knowledge concerning stone findings in the liver is by no means a recent one. The literature on this topic is rather instructively collected by Beer,[3] in his paper, to be referred to later. Intrahepatic stones are on record as far back as 200 years ago or over, and according to Courvoisier's collection in 1891, the number of the listed cases amounted to 50, while Beer in 1904 makes reference to 150 cases. Of course many of these reports could not stand careful scrutiny, as we shall point out later.

In view of the fact that stones in the gallbladder were found as frequently as up to 10 per cent of all the autopsy material; furthermore, that in a considerable percentage of such cases intrahepatic stones were detected (according to Schroeder, Beer in about 8–9 per cent, according to Peters, Huenerhoff in about 1 per cent of the extrahepatic lithiasis), one might have concluded that intrahepatic stones are not very rare occurrences, and careful postmortem examination should have undoubtedly materially increased the incidence of intrahepatic stones.

Intrahepatic stone formation is considered a secondary process, following a primarily existing extrahepatic lithiasis. The type and character, as well as the chemical composition of the stones in the liver, are practically always identical with the ones found in the gallbladder.

In all the 6 cases of Beer and in practically all the other cases quoted by him on reviewing the literature (Naunyn, Kehr, Riedel, Czerny, and others), there was present simultaneously with the intrahepatic stones also an extrahepatic stone formation (cholelithiasis, impacted stone in the common duct, cholangeitis, etc.). In none of the cases presented was there any convincing evidence of the existence of intrahepatic stones without the participation of the gallbladder. In the recently published case of Koster and Gerber,[8] both extrahepatic and intrahepatic lithiasis were simultaneously present. Graham, Cole, Copher, and Moore[5] also note that hepatic stones, with simultaneous stone findings in the extrahepatic biliary passages, are not rare occurrences, "it is rare however for stones to be located in the hepatic ducts alone." This is their only remark regarding intrahepatic stones. No hepatic stones are mentioned in any relation in the well-known textbooks of Assmann,[2] Carman,[4] Jordan,[7] Matthes,[12] Meyer,[13] Stierlin,[14] McKendrick and Whittaker,[11] Holmes and Ruggles,[6] and Lyon[10] among others.

In 2 cases presented here, intrahepatic stones were found in individuals, who had not suffered from calculi in the gallbladder. In both cases there was a genuine, primary, localized stone disease, affecting the smaller hepatic branches or radicles, without any generalization in that organ, or *without the participation of the gallbladder in the process*. These cases should accordingly be classified as principally "intrahepatic lithiasis," in contrast to the intrahepatic stones, where the origin and formation place of the stones remain open to question.

Diagnosis in both of our cases has been made intra vitam by means of roentgenog-

raphy, in contrast to the general rule in which no intra-vitam diagnosis but only post-mortem incidental findings detected the presence of biliary calculi in the smaller biliary passages. In both cases also surgical procedures were performed, in the first one prior to diagnosing the intrahepatic lithiasis, in the second case, following it.

## CASE REPORTS

Case 1. I. L. female, aged forty, Russian Jewess, first seen at our office on November 12, 1928, referred by the surgeon who had performed a cholecystectomy six months prior to that date. Patient had been suffering for four years prior to this operation. The pain, as described, was typical of cholelithiasis, the attacks coming on first at rarer, later at more frequent intervals. During the year preceding operation, the pain never subsided. Diet and medicines were of no help.

The surgeon removed the gallbladder, which however did not contain any stone. Patient felt perfectly relieved after the cholecystectomy for about six months, when, about two weeks before she first came to our office, complaints recurred again, with the same type and severity of the pain as existed before the operation. Patient lost 10 lb. during the last two weeks.

Fig. 1. Case 1.

The surgeon, puzzled by the recurrence of painful attacks, re-hospitalized the patient. After the hospital stay, no diagnosis being established, the patient was referred to us.

Physical examination failed to show any obvious pathological condition. Even the liver and gallbladder region proved to be free of any abnormal findings.

Roentgen examination, however, detected the presence of certain shadows on the films taken of the liver region. This shadow proved to be identical on each of the films taken at different times and under various techniques, and was similar to the well-known bilirubin calcium stone shadows, such as are often found in the gallbladder. The stones were distinguished by their opaque calcium content; the individual stones were of a pinhead or cherry pit size, and of uniform shapes, grouped in cluster formation, the mass being approximately the size of a walnut, located within the shadow of the liver in the medio-clavicular line, at the height of the 12th rib (Fig. 1).

After excluding all possible diagnoses such as stones in the gallbladder (the gallbladder had been removed previously) or in the renal pelvis, calcified glands, calcification of the cartilages of the ribs, ossification in the scar tissue, desmoid and dermoid tumors, teratoma, calcified echinococcus cyst, foreign bodies, iodeikon free or in gelatine capsules, diverticular barium retention in the colon, drugs, etc., we made a diagnosis of intrahepatic stones.

Case 11. N. G., female, aged thirty-one, Italian, came to our office on October 25, 1930, with the chief complaint of incessant vomiting of two months' duration. Patient vomited after each meal, several times daily. The vomited mass was described as sour, not containing any stagnant food. It has never been tarry or bloody; 16 lb. loss of weight. Complete anorexia; general weakness. No pain of any nature, nor any other complaints were mentioned.

In the past history somewhat similar vomiting spells were referred to; the first one about fifteen years ago was of a duration of nearly five years, and another one, three years ago of a duration of a few months. Appendectomy had been performed five years ago.

Clinical examination, including pelvis, was negative.

Ewald test meal revealed normal acidity and motor power.

Roentgen examination of the gastrointestinal

tract was negative. The gallbladder did not give any shadow on the flat plate. After the Graham-Cole test, the gallbladder was visualized, and was of a normal contour and appearance. The dye concentration power was slightly diminished. No pathology, such as adhesions or stones was noted. After the administration of fat-containing food, the gallbladder contracted, probably less promptly and to a lesser extent than normal.

While the gallbladder region seemed to be negative, the liver contained a multiple stone shadow similar to the one described in the first case, being different only in regard to its location. The cluster of stones was located between the 11th and the 12th ribs, near the outer border of the liver (Fig. 2).

Medical treatment resulted only in transitory improvement as manifested by the cessation of the vomiting and some gain in weight. The presence of the intrahepatic stones could, in our opinion, hardly explain the clinical picture as described. A causal correlation seemed to us too inconclusive. Although the intrahepatic stones seemed, a priori, not easily amenable to surgery, still, after both symptoms, vomiting and loss of weight, following the initial improvement in the general health, recurred again, at the patient's request an exploratory laparotomy was decided upon.

At the operation the stomach and the duodenum proved to be normal. The appendicular region exhibited some slight adhesions, which were released. The gallbladder showed an unusual fatty yellow appearance: a fatty infiltration of its wall. It was densely filled, without any visible pathology, adhesions or palpable stone findings. The surgeon and both of his assistants were able to easily palpate the stones, as visualized on the films, located on the lower surface of the liver, near the edge. They were not removed.

The gallbladder, though apparently without any pathology, was removed and seemed to be normal, but contained a pure cholesterol stone of an almond size, with sharp edges and surfaces, with a crystalline, glistening, brilliant, translucent character and light yellowish color. This stone, in the gallbladder as well as after its removal, gave no (positive nor negative) shadow on the roentgenograms, its absorption power possibly equalling the surrounding bile, as is usually the case with cholesterol stones.

Patient felt all right after the operation, until about six weeks later, when vomiting and anorexia recurred again.

Fig. 2. Case II.

## COMMENT

Two cases are reported with circumscribed, cluster-shaped intrahepatic stone shadows, as detected in both cases by roentgenography and confirmed in the second case by operation. In both cases the intrahepatic stones must be considered as expressions of genuine intrahepatic lithiasis, because simultaneously with the presence of stones in the hepatic ducts, no other stone formation or location in the biliary system could be found.

In case of intrahepatic stones with a simultaneous extrahepatic lithiasis, the place of origin for the intrahepatic stones may be questioned. They may have been formed in situ, within the intrahepatic ducts, or they may have been carried there from the extrahepatic passages. However, in both of our cases, the extrahepatic passages were free (from inflammation and similar stones), and they as the source of formation of the intrahepatic stones could hardly come into question.

In the first case, six months prior to the calculous findings, the gallbladder had been removed, and no stone was found in the gallbladder or in the common duct. In the second case, the gallbladder was removed and found normal, without any sign of inflammation or other pathology, as was the common duct. This undoubtedly incidental finding of a solitary cholesterol stone in the gallbladder as expression of certain metabolic disturbance points to an entirely different etiology from the one which produced the small multiple calcium bilirubin stones in the hepatic ducts, as expressions of chronic inflammatory process. The absence of any inflammation in the gallbladder rules out the possibility of the extrahepatic passages as the formation place of the stones detected within the hepatic ducts. Consequently both cases represent the unique type of a renal intrahepatic lithiasis when the stones found in the hepatic ducts were also produced there. Their existence was not co- nor subordinated to a simultaneously, in fact, primarily existing extrahepatic stone formation, as is the case in the majority of all the cases described in the literature.

In view of the extremely rare occurrence of a genuine and solitary intrahepatic lithiasis as herein described, questioning the diagnosis, especially with respect to the interpretation of the roentgen findings, seems to be perfectly justifiable. However, the picture of a typical shadow was a constant and identical finding on all the films, though various techniques, postures, time factors, etc., were employed, and all the possible differential diagnoses were carefully considered. Consequently both the direct and also diagnosis by exclusion tended to substantiate and to corroborate the diagnosis.

Accepting the diagnosis of intrahepatic stones, in fact, that of an intrahepatic lithiasis, it is of more than merely academic interest to analyze the question, whether this latter represented solely an incidental finding or whether the complaints referred to were in causal relation with these findings. In other words, whether the patient suffered from the intrahepatic stones, i.e., the complaints were caused by the intrahepatic lithiasis, or there were other conditions responsible for these symptoms, and the stone finding was only incidental.

It is generally known that stones may be lodged in extrahepatic passages for a very long period, even for a life time, without causing any symptoms; possibly this may be the case in certain instances of intrahepatic localization of the stones, especially if the obstruction of the bile flow is incomplete (Murchison). This interesting fact can be contrasted with the dyskinetic attacks of cramps, i.e., cholelithiasis-like painful attacks occurring without inflammation or stone, in a purely reflex manner (Aschoff, Westphal). Accordingly in extreme cases stones may be present causing no symptoms whatsoever, and again, in absence of stones or inflammation cholelithiasis-like cramp may be complained of. Again, in other cases, intrahepatic stones may do more harm than the usual location of the stones in the extrahepatic passages. Pressure, pain, inflammation, icterus, decubitus, abscess, cholangitis, pylethrombophlebitis, etc., may result from the presence of stones in the hepatic passages, especially if the inflammation becomes active.

The next question is whether the stones found within the liver shadow were actually produced in situ, or whether they made their way there, either by migration, or by natural expansion.

In cases of obstructive processes of the common duct, caused by impacted stones, if the number of stones produced in the gallbladder is very large or the stones are growing in size by accretion, the latter may fill up the adjoining large biliary passages, and if still more room is required for the lodging of these stones, also the secondary branches of the biliary system may of necessity become filled with stones. This phenomenon can occasionally be observed during post-mortem examination.

This certainly was not the case in either of our cases.

In case of real "migration" of the stones, two paths are open. Intrahepatic stones may have access to the extrahepatic routes, and a small intrahepatic pigment concrement may serve as a nucleus for larger stone formation in the gallbladder, or again, gallbladder stones may wander through the cystic duct and make their way to the common or also the main hepatic duct or from the latter into the secondary biliary passages. This possibility also is excluded in our cases.

In any of the aforementioned possibilities it remains a natural prerequisite that the stones found in both the extra- and intrahepatic passages must show similar chemical and morphological qualities, although slight changes due to various, subsequent, recidivant stone formations may have their impregnation thereon.

In case of intrahepatic lithiasis the hepatic stones are produced in situ. It was reasonable for us to assume that both of our cases belonged to this group. And so this inference by exclusion leads to the same consideration as our clinical and direct conclusion leads, namely, that both cases represent genuine, primary intrahepatic lithiasis.

A further "indirect" way leads us to the same conclusion. The postulates, as formulated for the intrahepatic stone formation by Beer, comprise the following: an obstructive cholangeitis, due to impaction by stones—and not by tumor or any other pathology—in the common duct; a duration of two months or more; the presence of certain dyscrasia or disposition to stone formation. These postulates were encountered in all of Beer's cases and in most of the cases quoted by him from the literature, in which both intra- and extrahepatic stones were simultaneously present. In our cases intrahepatic stones were found without the participation of the extrahepatic passages, and none of Beer's prerequisites were present.

SUMMARY

Two cases of true, primary intrahepatic lithiasis have been reported, without the participation of the extrahepatic biliary system, in absence of the commonly known postulates to the stone formation in the liver.

In both cases diagnosis was made by roentgen examination.

The extreme rarity of this condition has been stressed.

A discussion has been given of the possible causal relation between the clinical symptoms and the intrahepatic stone finding.

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# WHAT THE RADIOLOGIST SHOULD KNOW ABOUT CLINICAL PATHOLOGY*

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PHILADELPHIA, PENNSYLVANIA

THE work of the radiologist brings him in intimate contact with every specialty in the modern practice of medicine. To keep abreast of the times in every specialty is obviously impossible, and yet the radiologist, to be regarded as a consultant, must of necessity be conversant with the fundamentals upon which the various medical specialties are based. Furthermore, intelligent roentgen interpretation is dependent upon a full appreciation of the significance of the clinical and laboratory data available in any given case. Only after careful correlation of the clinical, laboratory and roentgenological findings can an intelligent opinion be expressed regarding the significance of the roentgen changes.

Most radiologists in their efforts to master the art and science of roentgenology have neglected and forgotten much of the general knowledge of medicine that was taught them in the medical school. Furthermore, in most instances, many years separate the radiologist from his student days, and during these years numerous and noteworthy advances have been made in all branches of medicine. In his daily work, the radiologist finds himself constantly confronted by such a lack of general knowledge as to be a serious handicap to the efficient application of his specialty. In no branch of medicine is this deficiency more keenly felt than in clinical pathology. A working knowledge of the clinical significance of the various laboratory tests, both new and old, is of inestimable value to the radiologist. It is with the idea of supplying this working knowledge of clinical pathology, written for radiologists, from a radiological point of view, that this presentation is offered.

It is not intended to give a full and complete résumé of the present status of clinical pathology. The more elementary and generally known facts have been omitted. Such aspects of the subject as find most frequent application and are most universally employed have been selected and while not all are of direct interest to the radiologist, nevertheless they bear upon such important phases of medicine as to make them desirable possessions of every well-informed radiologist. It is further acknowledged that this presentation has not been strictly confined to clinical pathology since an attempt has been made to correlate the facts of clinical pathology with those of clinical medicine so that such knowledge may be of most practical value.

## I. THE BLOOD

Numerous and intensive investigations upon the blood have, in recent years, yielded rich rewards and have added much to our knowledge both in the field of hematology and in the biochemistry of the blood. It is our purpose to briefly review the more important phases of this subject, especially those aspects of particular interest to the radiologist. The nomenclature of hematology is replete with names and terms that are most confusing to the uninitiate. An attempt will be made to define such terms as are considered essential to a proper understanding of the subject.

### *A. The Cellular Elements of the Blood. Hematology.*

#### 1. *The Red Blood Cells—Erythrocytes.*

a. *Normal Values:* The normal number of red blood cells for the male ranges from 4,500,000 to 6,000,000 per c.mm. of blood. The range for females is slightly less—

* From the Department of Radiology and Medicine of the Graduate Hospital of the University of Pennsylvania, Philadelphia. Read at the Thirty-Sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

4,000,000 to 5,500,000. Various terms have been introduced to indicate the relative number of red cells in a given blood, thus *normocythemia* indicates a normal red cell count; *hypercythemia* a greater number than normal, and *hypocythemia* fewer than normal. These terms have been used by Haden in his classification of the anemias.

The *erythrocytes* (normocytes) have their origin in the bone marrow and are derived from nucleated cells, termed *normoblasts*. In the circulating blood will be found certain *immature erythrocytes* which differ from mature cells in their staining reaction. Whereas the mature red cell has a pinkish color when stained by Wright's or Wilson's stain, the immature cell will show a distinct bluish tinge. When this is diffuse throughout the cell the condition is spoken of as *diffuse basophilia* or *polychromatophilia*. When bluish granules are present the condition is termed *punctate basophilia* or *stippling*. Such stippling is of diagnostic importance in chronic lead poisoning. In this condition, however, the significance of such stippling is not clearly understood. The *reticulocyte* is another variety of immature erythrocyte. It shows filaments by vital staining and normally constitutes less than 1 per cent of the red cell count. An increase in reticulocytes is the earliest indication of regeneration of red cells by the bone marrow, and is also the first sign of the effectiveness of liver in the treatment of pernicious anemia. These cells are also especially numerous in familial hemolytic jaundice. An increase in number of any of the above immature erythrocytes is an indication of active red cell formation by the bone marrow.

The *nucleated erythroblasts* are precursors of the red corpuscles and do not normally occur in the circulating blood. (*a*) The *normblast* is the immediate precursor of the erythrocyte and is of approximately the same size. (*b*) The *macroblast* is an earlier form of normoblast and is a fairly large cell. (*c*) The *megaloblast* is a large nucleated erythroblast concerning which there is considerable dispute. It may or may not be a precursor of the normoblast. The appearance of megaloblasts in the circulating blood indicates a profound disturbance of bone marrow function. They are encountered chiefly in pernicious anemia.

Various terms are commonly employed to designate a pathological appearance of the red cells. Distortion in the shape of the erythrocytes is spoken of as *poikilocytosis*. Poikilocytes may occur in any severe anemia but especially in pernicious anemia. An oat-shaped or sickle-shaped cell occurs in sickle cell anemia. Variation in the size of the cells is termed anisocytosis. The size or volume of the red blood cell is of importance since upon its volume will depend the hemoglobin content. Variation in size may be due to a change in diameter or thickness of the cell. Normal cells measuring 7.5 microns are known as *normocytes*, cells smaller than 5 microns are *microcytes*, while those larger than 10 microns are *macrocytes* and very large cells are *megalocytes*. In certain anemias the red cells are predominantly of one size, thus giving rise to the terms normocytic, microcytic, macrocytic and megalocytic anemia. Post-hemorrhagic anemia is an example of the normocytic type, secondary anemias are usually of the microcytic variety while in pernicious anemia there is a marked macrocytosis.

The size or volume of the red corpuscle is obtained by determining the *volume index* which represents the relative volume of the individual red cells as compared with those of normal blood. The normal range of the volume index is 0.85 to 1.0. It is of considerable value in the diagnosis of pernicious anemia since it is nearly always increased in this disease and rarely in any other condition. In secondary anemias the volume index is usually diminished.

b. *Hemoglobin:* The most important constituent of the red blood corpuscles is hemoglobin, with which they are saturated to the extent of 33 per cent of their volume. It is very rare for them to be deficient in hemoglobin. The erythrocytes are broken down in the liver, spleen and circulating

blood and the liberated hemoglobin is utilized by the spleen and liver in the reconstruction of the blood. The older method of estimating the hemoglobin content of the blood in percentage is very unsatisfactory inasmuch as there is considerable variation in the standards of the different types of hemoglobinometers used for this purpose. It is much more accurate to determine the number of grams of hemoglobin per 100 c.c. of blood. This method is rapidly replacing that in which the hemoglobin is reported in percentage. The normal values of hemoglobin are for the male 14 to 18 grams per 100 c.c. of blood, and for the female, 12 to 15.5 grams. For those who still prefer the percentage method, this can be obtained by multiplying the number of grams of hemoglobin by 6.

The *color index* of a given blood represents the relative amount of hemoglobin per individual red blood cell as compared with that of normal blood. The normal range of the color index is 0.85 to 1.0. A color index above 1.0 is characteristic of pernicious anemia while a low index occurs in chlorosis and most cases of secondary anemia. A decided variation in the color of the individual red cells has been termed *anisochromia*. Cells of normal color are normochromic. Cells showing a decrease in color are said to be hypochromic, while those of unusual pallor are achromic. These changes may be due to a decrease in the amount of hemoglobin but is more frequently the result of an unusual thinness of the cell. Likewise extremely thick cells will appear unusually dark, *hyperchromic*. Such cells are common in pernicious anemia, while achromia is characteristic of chlorosis and some types of secondary anemia. On the basis of color, we may therefore have a normochromic, hypochromic, or hyperchromic anemia.

c. *Sedimentation Rate:* For some time it has been known that under the influence of various diseases there is acceleration in the rate with which red corpuscles settle out of blood prepared so that it will not clot. Recently, advantage has been taken of this fact in the diagnosis and prognosis of various conditions, and, although there are still many phases of this subject which require clarification, the study of the sedimentation rate has been of great value.

The test can be done either by determining how quickly the blood cells settle to a given level in a standard tube or by measuring the distance that they fall in a given time. As usually performed in this country, the latter method is employed. It is necessary to correct for anemia, since it has been shown that apparent acceleration of the sedimentation rate takes place if the number of cells per unit of blood volume is decreased. If correction is made for anemia, the normal sedimentation rate, that is, the number of millimeters the blood will settle in a standard tube in one hour, is usually 3 to 5 mm. and the upper limit of normal is 10 mm. The sedimentation rate is increased in the presence of acute and chronic infections of all types. There is, therefore, nothing specific about this test. It is of great value, however, in following the course of an infection and is of particular worth in determining the degree of activity of pulmonary tuberculosis. The sedimentation rate very often remains increased after all other signs of activity have disappeared. In the study of tuberculosis, determinations of the sedimentation rate are of great assistance in conjunction with the roentgen examination of the chest. It has also been shown that most instances of malignancy are associated with increased sedimentation, so that this laboratory procedure frequently aids in the differential diagnosis of tumors.

d. *The Anemias:* Recent researches upon the blood and blood diseases have very materially changed our concepts regarding the anemias. Ottenberg, in an excellent review, gives a résumé of the noteworthy experimental work that has been done in recent years upon this subject. As the result of such investigations a better understanding of the nature and production of the various types of anemia is afforded.

It is important to remember that anemia is not a disease but a symptom that is common to a variety of conditions. It is usually the result of injury or insufficiency of the blood-forming organs, rather than any disturbance in the circulating cells of the blood. However, a study of the blood will often reveal the nature of the bone marrow disturbance and may indicate the etiological agent responsible for the condition. The function of the red blood corpuscles is to carry oxygen from the lungs to the tissues, and since this function is the property of the hemoglobin an estimation of the hemoglobin content of the blood becomes of prime importance. In the estimation of the hemoglobin content, three factors are to be taken into consideration: the number of red cells, the size (volume) of the red cells, and the hemoglobin content of each cell. A deficiency of hemoglobin, which constitutes what is commonly termed "anemia," may, therefore, be due to any one of three factors: too few cells, cells that are too small or cells which do not contain sufficient hemoglobin. This latter condition is very rare. Therefore, in the detection and determination of the type of an anemia, one must know the red cell count, the volume index (size) and the color index (hemoglobin content per cell).

Anemia is a symptom with which every practitioner is more or less constantly confronted. The radiologist finds it as an important complication in many patients suffering from cancer, and thus he has a direct interest in this subject. The rapid advance in our knowledge has brought about the necessity of reclassification of the anemias. Ottenberg's new classification, given in part in Table 1, is based chiefly upon pathogenesis and response to treatment.

*Anemias due to various deficiencies:* The anemias resulting from various deficiencies are those which are best understood and which have given the most gratifying therapeutic results, since supplying the deficient substance usually suffices to cure or check the anemia. Iron has long been recognized as a prime factor in the treatment of anemia, yet until recent years little has been known regarding the manner and mechanism of iron utilization by the body. As the result of recent knowledge iron therapy has been placed upon a more rational basis. Anemias resulting from simple loss of blood such as occurs in carcinoma of the uterus, malignancy of the gastrointestinal tract and peptic ulcer are now recognized as due essentially to iron deficiency. Those anemias in which iron deficiency is a basic factor are termed *hypochromic anemias*. In this category is *chlorosis*, which is an example of a normocythemic, normocytic and hypochromic anemia, having cells normal in number and size but deficient in color.

Table I

OTTENBERG'S NEW CLASSIFICATION OF ANEMIAS

Anemias due to:

I. Deficiencies.
   A. Iron deficiencies.
   B. Deficiency of "antianemic principle."
   C. Nutritional deficiencies.
II. Injury to the blood-making organs.
   A. Toxic destruction of marrow.
   B. Mechanical replacement of marrow.
   C. Interference with blood regeneration at some intermediate stage.
III. Disintegration of blood. (Hemolysis.)
   A. Caused by hereditary defects of red blood cells themselves.
   B. Toxic destruction of blood.

Probably the most noteworthy contribution to our knowledge of the anemias is the recognition of an "*antianemic principle*," due largely to the work of Minot and Murphy. These investigators, stimulated by the prior researches of Whipple and Robscheit-Robbins, found that liver is practically a specific for pernicious anemia. The substance in liver which combats the anemia is referred to as the "antianemic principle." There is now recognized a group of anemias due to a deficiency of the antianemic principle of which pernicious anemia is by far the most important.

There has long been recognized, as an essential part of pernicious anemia, an absence of hydrochloric acid in the stom-

ach. It has been found that without exception achlorhydria precedes all other symptoms of the disease. Castle and his coworkers, investigating the relationship of achlorhydria to pernicious anemia, found that when chopped meat was first thoroughly digested with gastric juice and then administered to pernicious anemia patients, it was as efficacious as the administration of liver. It is therefore recognized that the antianemic principle consists of some substance found in normal gastric juice (intrinsic factor) and another essential substance supplied by beef muscle and certain other foods (extrinsic factor). The combination of these two substances in the stomach produces the antianemic principle. When absorbed, it is stored in the liver and thus accounts for the efficacy of the administration of liver in pernicious anemia.

Probably no disease presents more profound blood changes than does pernicious anemia. It affords our best example of a hypocythemic, macrocytic and hyperchromic anemia, having a marked reduction in the number of red cells which are larger than normal and darker in color. The red cell count is frequently less than 2 million. The disease is characterized by a poikilocytosis and especially an anisocytosis, there being numerous macrocytes present. The color and volume index are both increased above 1.0. The platelets are much reduced in number, as are also the leukocytes. With the onset of a remission many immature red cells appear, first the reticulocytes and then the polychromatophilic and stippled red cells. Nucleated erythroblasts may appear, both normoblasts and megaloblasts, when there is marked bone marrow activity. The megaloblasts are usually few in number but their presence is of great diagnostic significance since they are rarely found in any other condition.

Under *nutritional deficiencies* is to be found a large group of anemias due to deficiencies of the various vitamins and food elements and the anemias accompanying biliary, duodenal and pancreatic fistulae. No doubt the anemia so commonly found in certain malignancies is on the basis of a nutritional deficiency, especially those of the gastrointestinal tract. Intensive irradiation of malignant lesions of the mouth, pharynx and larynx by the so-called Coutard method which is being so extensively used at the present time results in considerable interference on the part of the patient to take proper nourishment. An anemia resulting from nutritional deficiency might readily occur in such patients.

*Anemias due to injury to the blood-making organs:* Under this heading will be found many diseases of special interest to the radiologist. *Toxic destruction of the bone marrow* results in aplastic anemia (deficiency of red cells, white cells and platelets). Radium and thorium are definitely known to produce this form of anemia. The therapeutic use of radium water has practically been discontinued since the report of several cases of fatal radium poisoning. The fear of producing an aplastic anemia has been used as a contraindication for the intravenous use of thoratrast (thorium dioxide) as a contrast medium in roentgenography. As yet there is no substantial proof that thorium used in this manner is injurious to the blood or bone marrow. While intensive irradiation with roentgen rays or radium may so affect the normal bone marrow as to produce an aplastic anemia, irradiation need never justifiably be carried to such an extent. In conditions showing pathologic conditions of the bone marrow, irradiation should be given with extreme caution.

Practically all the diseases producing *anemia by the mechanical replacement of bone marrow* have some radiological implication. Thus the various osteoscleroses, including the marble bone disease of Albers-Schönberg, are usually first recognized by a roentgenographic examination of the bones. Gaucher's disease and xanthomatosis or the Schüller-Christian syndrome have a characteristic roentgenographic appearance. Leukemia, Hodgkin's disease and metastatic malignancy of the

bone, the accompanying anemia of which results from bone marrow replacement, are of vital interest to the radiologist. It is well for the radiotherapist to remember that in these pathologic conditions of the bone marrow, irradiation, if carried too far, might readily produce an aplastic anemia. Fortunately, it is a well-recognized principle in the treatment of these conditions, especially leukemia and Hodgkin's disease, that they will respond, if at all, to small doses of roentgen therapy and that treatment should be given as infrequently as possible.

The *anemias due to interference with blood regeneration at some intermediate stage* concerns diseases of the spleen and liver such as Banti's disease, cirrhosis of the liver and prolonged obstructive jaundice. Since the liver and spleen are intimately concerned in conserving the material resulting from the disintegration of red blood cells and subsequently utilize this material for the reconstruction of the blood, any condition which interferes with this specific function of these organs will produce an anemia.

*Anemias due to disintegration of the blood* (hemolysis)*:* Hemolysis may be the result of a *hereditary defect of the red blood cells* or a *toxic destruction of these cells*. In the former group are two diseases—hemolytic icterus and sickle cell anemia, which resemble each other clinically but can be differentiated on the basis of the fragility of the red cells. According to the fragility test normal red cells in salt solution show no hemolysis until the concentration of the salt is reduced to about 0.44 per cent. In hemolytic jaundice, the cells may begin to dissolve in concentrations of 0.5 to 0.6 per cent. Complete hemolysis may occur in concentrations of 0.4 to 0.48 per cent as compared with 0.34 per cent for normal cells. Such increased fragility is not seen in sickle cell anemia, the fragility test being either normal or decreased. Sickle cell anemia may at times show striking changes in the bones roentgenologically.

There are many toxic agents which may produce anemia by hemolysis. In this category are to be found diseases due to various bacteria and protozoa, including malaria and syphilis. Hemolysis may occur as the result of a large variety of chemical agents. The anemia complicating nephritis and extensive burns is thought to be due to some hemolytic agent. The anemia of cancer is also attributed to toxic destruction of the red cells, although such a toxin has never been definitely demonstrated.

e. *Polycythemia:* This is a condition in which there is an increase in the number of red blood cells in the circulating blood, which may be relative or absolute. A *relative polycythemia*, better termed *erythrocytosis*, is a condition in which the red cells per cubic millimeter are increased but the total number in the body remains normal. An erythrocytosis of 6 to 7 million may occur in apparently normal individuals. Such counts may also be encountered in dehydration from severe vomiting, diarrhea or sweating. An *absolute polycythemia* exists when the total number of red cells of the body is increased, as well as their concentration in the blood. It indicates a stimulation of the bone marrow to the overproduction of red cells. Absolute polycythemia may occur as a symptom in a variety of conditions and in polycythemia vera.

Polycythemia is found in normal individuals living at high altitudes and is thought to be due to the low oxygen tension which stimulates the bone marrow to increased activity. It occurs in myocardial insufficiency in which there is chronic cyanosis, with counts reaching as high as 7 to 8 million. In this condition, it is interesting to note that chronic passive congestion of the lungs resulting in pulmonary fibrosis may present a roentgen appearance that simulates pneumoconiosis. Polycythemia will also be found in long standing pulmonary disease such as emphysema, pulmonary fibrosis and any condition interfering with pulmonary ventilation. Also, chronic poisoning with a variety of drugs such as arsenic, phosphorus, radium and mercury

will produce an increase in the red cell count, while recovery from any severe anemia usually results in a transient erythrocytosis. It is interesting to note that most radiologists and technicians show a tendency to an erythrocytosis.

*Polycythemia vera, erythremia, Vaquez-Osler's disease* is a chronic incurable disease. It is characterized by an absolute polycythemia, the red cell count usually exceeding 8 million, although occasionally it may reach only 5 to 6 million. Counts from 12 to 15 million have been reported. The hemoglobin is increased to 120 to 150 per cent. The color index is below 1.0 and the cells tend to be small and pale. There is usually a moderate neutrophilic leukocytosis, 10,000 to 15,000. The blood platelets are usually increased. The pathological change found in erythremia is an extreme hyperplasia of the blood forming tissues of the marrow. In the treatment of erythremia, roentgen irradiation of the long bones is recognized as one of the most valuable methods of therapy.

2. *The White Blood Cells—Leukocytes.*

a. *Normal Values:* The normal number of leukocytes may range from 5,000 to 10,000 per c. mm. of blood. There are three distinct varieties of white cells: the *granular leukocytes*, the *lymphocytes* and the *monocytes*. The granular leukocytes, because of their origin from the bone marrow, are sometimes called *myeloid leukocytes* or more simply *granulocytes*. Of these cells, there are three varieties, the *neutrophiles*, the *eosinophiles* and the *basophiles*. Because of the lobulated appearance of the nucleus these cells are also called *polymorphonuclear leukocytes*.

The function of the neutrophiles is to combat infection, which they do by engulfing and digesting bacteria. They may also take up small foreign bodies. Because of this property, they are termed *phagocytes*. The function of the eosinophiles is not definitely known. Since they are increased in diseases associated with protein hypersensitiveness and during infestation with animal parasites, it is assumed that their function is concerned with the removal of foreign protein and combating parasites. The function of the basophiles is not known and relatively little is known regarding the function of the lymphocytes. They are probably concerned in the defense against chronic infections, particularly tuberculosis. The monocytes are phagocytic, acting as the scavengers of the blood, taking up damaged red cells and disintegrated leukocytes. They are known as *macrophages* in contradistinction to the smaller neutrophiles, the *microphages*.

Inasmuch as these various types of leukocytes apparently have different functions, it is not sufficient merely to know the total number of leukocytes but one must also know the number of each variety or the *differential count* as it is termed. It has long been the custom to express the differential count in percentages of the total number. It would seem preferable and more precise to indicate the actual number of each type of cell, as advocated by Kolmer, Boerner and Garber. Table II gives the normal range of leukocytes with variations for age.

Table II

NORMAL RANGE OF LEUKOCYTES*

| | 3 months to 3 years | 3 to 5 years | Over 5 years and adults |
|---|---|---|---|
| Neutrophiles | 2000–7000 | 3000–8000 | 3000–7000 |
| Basophiles | 0–50 | 0–50 | 0–50 |
| Eosinophiles | 25–700 | 50–700 | 50–400 |
| Lymphocytes | 4000–9000 | 2500–6000 | 1000–3000 |
| Monocytes | 25–700 | 25–700 | 100–600 |

*Kolmer, Boerner and Garber

b. *Origin of the Leukocytes:* It is essential to know the origin of the various types of white cells, since this enables one to understand certain features of the different blood conditions in which the leukocytes play an important rôle. The granulocytes and monocytes arise from certain immature cells which have their origin in the bone

marrow. The precursors of the lymphocytes originate in the lymphoid tissue scattered throughout the body. The immature leukocytes in themselves are not abnormal; it is their appearance in the circulation that is pathological.

(1) *The granular leukocytes:* Since the precursors of these cells arise within the bone marrow they are known as myeloid cells. The earliest recognizable ancestor of the mature granulocyte is the myeloblast. the metamyelocyte, which represents about 4 per cent of the neutrophiles. The three most immature forms including the myelocyte are not phagocytic and show little or no motility. Thus when they occur in the blood under pathological conditions they afford no protection against infection which is one of the chief functions of the mature granular leukocytes.

(2) *The lymphocyte:* The immature lymphocyte is known as a lymphoblast and is

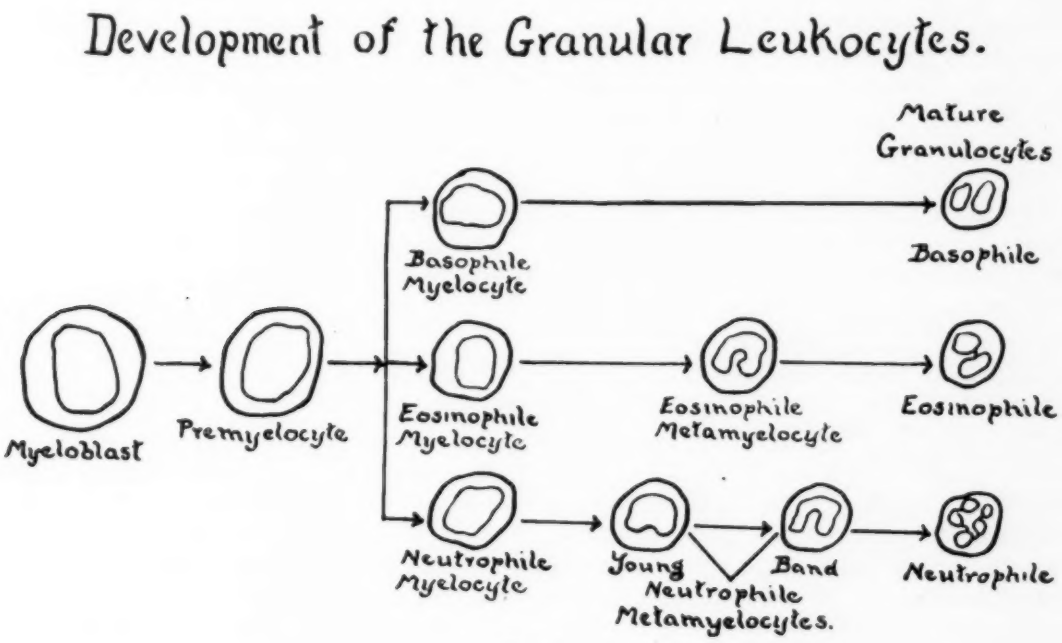


Fig. 1

Proceeding toward maturity we have next the premyelocyte and then the myelocyte. There are three varieties of myelocytes: the neutrophilic, eosinophilic and the basophilic. The neutrophilic myelocyte next becomes a young metamyelocyte, then a "band" metamyelocyte and finally a mature neutrophile, while the eosinophilic myelocyte becomes a metamyelocyte and then a mature eosinophile. The basophilic myelocyte passes directly into a mature basophile (Fig. 1). These various immature cells differ from each other as regards their size, presence of a nucleolus, staining qualities and character of the nucleus. None of them occur normally in the blood except a much larger cell than that found in the blood. The plasma cell, which is thought to be lymphatic in origin, is not a precursor of the lymphocyte but a collateral cell. A few such cells may be found in any condition in which the lymphocytes are in creased.

(3) *The monocyte:* The immature monocyte, if it occurs in the blood stream, cannot be recognized with certainty.

c. *Leukocytosis:* An increase in the total number of leukocytes of the blood above 10,000 per c.mm. is designated as a leukocytosis. An increase in number may predominantly involve only one of the several varieties of leukocytes, thus a differential count is important.

(1) Neutrophilia implies a neutrophilic leukocytosis and, since these cells predominate in the vast majority of instances, the simple term leukocytosis usually refers to a neutrophilic increase. Neutrophilia occurs in the following conditions: (1) acute infections, with several noteworthy exceptions such as typhoid fever, malaria, measles and influenza; (2) certain intoxications as uremia, lead poisoning and gout; (3) following acute hemorrhage; (4) pregnancy; (5) postoperative leukocytosis; (6) malignant growth, especially those involving the liver, gastrointestinal tract and metastases to the bone marrow; (7) acute and chronic myeloid leukemia.

(*a*) "*Shift to the left*": In cases of leukocytosis, especially acute infections, immature neutrophiles appear in the blood. The greater the percentage of immature forms, the greater is the degree of bone marrow stimulation. This increase of immature cells is called the "shift to the left." Attempts have been made, notably by Arneth, to utilize this fact in determining the degree of severity and prognosis of infections. The Arneth index has largely been replaced by the simpler and probably more accurate *Schilling index* in which an increase in the percentage of immature forms of leukocytes constitutes a "shift to the left." The greater the "shift to the left" the more severe is the infection, the less adequate is the response of the marrow and the graver the prognosis.

The "shift to the left" may also be indicated by determining the *nuclear index* (Boerner). This is the same as the Schilling index except that it is reversed so that a whole number is obtained instead of a fraction. The total number of mature neutrophiles divided by the total number of immature cells gives the nuclear index which for the normal adult is 15 or over. An index of 10 to 15 indicates a very slight shift to the left, 5 to 10 a moderate shift, and under 5 a marked shift to the left. The significance is the same as for the Schilling index. A "shift to the right" occurs only in pernicious anemia.

Some hematologists make a distinction between filament and non-filament types of neutrophiles, the filament being the connection between the various lobes of the nucleus. The non-filament forms are the more immature cells. Such a distinction results in a greater "shift to the left" than is obtained when this variation in nuclear structure is not considered. Similar differences in computing the nuclear index is responsible for the fact that the "shift to the left" in different hospitals and laboratories is not comparable. It becomes of value only when compared with counts made by the same laboratory.

(2) *Eosinophilia:* An increase in the number of eosinophiles above 3 per cent constitutes an eosinophilia. The causes of eosinophilia can usually be classified in three groups: (1) infestation with animal parasites, (2) skin disease, (3) reactions to foreign protein in hypersensitive individuals.

(3) *Basophilia:* This is of no known diagnostic value.

(4) *Lymphocytosis:* An increase in the lymphocytes is to be found in (*a*) normal infants after the first week, which may persist for the first few years of childhood; (*b*) certain infections, notably the early stages of whooping cough, German measles, mumps and in cases of uncomplicated tuberculosis of moderate severity running a favorable course; (*c*) convalescence from infections; (*d*) intoxications of various kinds; (*e*) lymphoid leukemia.

Of special interest in this connection is the disease known as *infectious mononucleosis* or *glandular fever*. This is an acute infection of unknown etiology occurring chiefly in children and young adults, characterized by fever, sore throat and marked swelling of the cervical glands. At times there may be a generalized adenopathy which along with the increase in lymphocytes may be mistaken for acute lymphoid leukemia, from which it differs in that no immature lymphoblasts are present. Characteristic of the disease is the abnormal morphology of the lymphocytes. The white

cell count usually ranges from 12,000 to 20,000, with the lymphocytes reaching as high as 85 per cent in the differential count. The disease runs a benign course of two to three weeks' duration. The term mononucleosis has nothing to do with the monocytes, which may or may not be increased in this disease.

(5) *Monocytosis:* An increase in the monocytes of the bood is rather uncommon and appears to be of no particular diagnostic significance.

d. *Leukopenia:* A decrease in the total number of leukocytes of the blood below 5,000 per c.mm. is designated as a leukopenia. This may occur in the following conditions: (1) cachectic and debilitated states, (2) certain infections as typhoid fever, measles, influenza and malaria, (3) agranulocytosis, (4) various intoxications as chronic benzol, acetanilid and arsenic poisoning, (5) exhaustion of the bone marrow as in pernicious anemia, terminal stage of chronic leukemia and bone marrow invasion by malignancy. A leukopenia is commonly observed in patients receiving intensive irradiation by radium or roentgen rays. It seems inadvisable to permit the granular leukocytes to fall below 3,000, since such patients show poor resistance to infection and also because of the danger of producing agranulocytosis. Radiologists and radiological technicians usually show a definite reduction in the number of white cells of the blood. Seldom does the count fall below 5,000. Here again it is important to watch the total number of granulocytes. The personnel of a radiological department should have a complete blood count at least every three months.

e. *The Leukemias:* Leukemia is a disease characterized by a hyperplasia in either the myeloid or lymphoid tissues of the body, resulting in a marked increase in number of the leukocytes and the appearance in the circulating blood of immature leukocytes. There are two distinct types of the disease, myeloid leukemia and lymphatic leukemia. Both may present an acute and a chronic form. An abrupt onset with the disease running its course in three to four months may be regarded as acute. The etiology is unknown, some regarding the disease as infectious, others, as neoplastic in origin.

(1) *Chronic myeloid leukemia:* This is the most common variety of leukemia and rarely occurs below the age of twenty. Because of the enlargement of the spleen the condition is also referred to as *splenomyelogenous leukemia.*

The blood picture in chronic myeloid leukemia presents an extreme degree of leukocytosis, the count usually ranging between 50,000 and 600,000. The vast majority of the cells are neutrophilic leukocytes. While most of these are mature, there are many of the immature forms. The myelocyte is the characteristic cell of this disease, constituting 20 to 50 per cent of the total leukocyte count. An occasional premyelocyte and myeloblast may be present. The eosinophiles and basophiles are increased in absolute numbers and often in percentage as well, while the monocytes are moderately increased in the early stage of the disease. The percentage of lymphocytes is greatly reduced, while the platelets show a marked increase. The red cells and hemoglobin reveal a progressive anemia of marked degree. A characteristic feature of the disease is the presence of numerous normoblasts.

The most effective therapy in chronic myeloid leukemia is roentgen or radium irradiation. It should be given as soon as the diagnosis is made. Therapy will be considered here only as it is influenced by the blood picture. Remission is usually prompt, but irradiation is increasingly less effective with each relapse. Aside from other considerations, irradiation should be resumed when the white count exceeds 100,000 or when there is an increase in the percentage of immature forms. Irradiation should be stopped when the total leukocyte count approaches normal and no more radiation than is required to accomplish this should be given. In the terminal stage of the disease, the symptoms and blood changes may

be similar to those of acute myeloid leukemia, and at this time irradiation is contraindicated.

(2) *Acute myeloid leukemia:* This is quite rare and is usually seen in children and young adults. The characteristic feature of the blood is the predominance of the extremely immature leukocytes, myeloblasts rather than myelocytes. In fulminant cases the leukocyte count may be diminished, the diagnosis depending upon the demonstration of myeloblasts. Such cases are known as *acute aleukemic leukemia* or *leukopenic leukemia.* The disease is often confused with acute septic infection. There is no effective form of therapy. Irradiation is contraindicated.

(3) *Chronic lymphatic leukemia:* This disease is less common than myeloid leukemia. It also occurs chiefly in adults. The blood picture shows a marked leukocytosis but somewhat less than in the myeloid variety. The average count is between 100,000 and 200,000, but many cases range between 30,000 and 100,000, with the lymphocyte count between 90 and 99 per cent. The predominant cell is the small mature lymphocyte. There is always a certain number of immature lymphocytes or lymphoblasts. An anemia develops in the later stages of the disease. Normoblasts are rare in contrast to the large number of such cells to be found in myeloid leukemia. The blood platelets are normal early in the disease but reduced later.

Irradiation is the treatment of choice but is less effective than in myeloid leukemia. The indications for treatment are essentially the same in the two conditions.

(4) *Acute lymphatic leukemia:* This disease occurs in children. It is rapid in onset, assuming a distinct hemorrhagic diathesis. The blood shows a marked leukocytosis with the large immature lymphoblast predominating. The platelets are much diminished, and there is a rapid anemia with little evidence of blood regeneration. Death may occur within a few days and usually within ten to twelve weeks. Treatment is of no avail.

(5) *Special types of leukemia and allied conditions:*

(*a*) *Chloroma:* A rare disease which may resemble either myeloid or lymphoid leukemia, more frequently the former. The disease is characterized by local tumor masses, the tissues of which have a green color. These masses have a tendency to invade bone, especially those of the head and more particularly the orbital bones, thus producing a protrusion of the eyeball. The bone development makes roentgen examination of importance in this condition. The blood changes are those of an acute or subacute leukemia with a variable leukocytosis. Immature cells, usually myeloblasts, are common. The so-called *chloroma cells* are pathological myeloblasts. The disease is usually fatal within a few months.

(*b*) *Eosinophilic leukemia:* A chronic myeloid leukemia showing a preponderance of eosinophiles is an extremely rare condition.

(*c*) *Plasma cell leukemia:* A form of lymphoid leukemia in which plasma cells predominate, also very rare.

(*d*) *Monocytic leukemia:* Another rare form of leukemia in which large numbers of monocytes appear early in the disease.

(*e*) *Pseudoleukemia:* A term applied to certain cases showing a general glandular enlargement and enlarged spleen without leukemic blood changes.

(*f*) *Aleukemic leukemia:* Cases which are clinically leukemia with the exception that the total leukocyte count is not increased. This may be of the myeloid variety, when such synonyms have been applied as aleukemic myeloid leukemia, aleukemic myelosis and latent myeloid leukemia. When of the lymphoid type the following terms have been used—aleukemic lymphoid leukemia, aleukemic lymphadenosis and latent lymphatic leukemia.

(*g*) *Aleukia:* A term applied to a clinical syndrome characterized by an extreme generalized aplasia of the bone marrow, presenting a severe anemia, a leukopenia and a

marked reduction in platelets with a hemorrhagic diathesis.

(*h*) *Leukemoid reaction:* The occurrence of many immature leukocytes, especially myelocytes as a part of a leukocytosis, the result of some severe infection, has been termed a leukemoid reaction because the blood picture strongly suggests leukemia. Such a reaction is not uncommonly seen in pneumonia, scarlet fever and severe sepsis.

(*i*) *Leukosarcoma:* A case of lymphosarcoma in which a leukemic blood picture later develops.

(*j*) *Agranulocytosis, granulopenia, and agranulocytic angina:* A clinical syndrome that has received considerable attention in recent years. It is characterized by an acute onset with fever, ulcerative pharyngitis or stomatitis, an extreme neutrophilic leukopenia and a rapidly progressive course to a fatal termination. The blood picture shows a marked reduction in the number of granulocytes, below 1,000. They are very often entirely absent. It is important to remember that in agranulocytosis the total number of leukocytes may be normal. Usually, however, all varieties of leukocytes show a marked reduction, so that a definite leukopenia exists. There are usually no myelocytes or myeloblasts present. The red cells, hemoglobin and platelets are normal. Roentgen therapy has been used with some success in the treatment of this condition.

3. *Blood Platelets or Thrombocytes.*

a. *Normal Values:* The normal number of platelets has been variously stated as from 200,000 to 400,000. They are difficult to count, therefore only marked variations from normal are significant. The thrombocytes are really not cells but fragments of cell cytoplasm. They have their origin in the bone marrow from the giant cells, *megakaryocytes*, by pinching off of portions of their long cytoplasmic processes.

The blood platelets are essential for the normal coagulation of the blood. Their deficiency is a common cause of pathological hemorrhage. A reduction in the platelet count is to be found in purpura hemorrhagica, in the hemorrhagic types of certain infections, especially smallpox and diphtheria, and in certain blood diseases associated with multiple hemorrhages, such as acute leukemia and aplastic anemia. In some of these conditions the platelet count may fall to below 10,000.

b. *Coagulation of Blood:* This phenomenon is a complicated process and many factors are concerned. In the study of hemorrhagic diseases, not only is the platelet count important but the other factors concerned in this process must also be investigated. These include the bleeding time, the coagulation time, test for calcium deficiency and an observation as to the retractility of the clot.

(1) *Bleeding time:* The normal bleeding time is three minutes or less.

(2) *Coagulation time:* The coagulation time varies somewhat with the method employed for its determination. With most of the methods commonly used the normal coagulation time varies from two to twelve minutes.

(3) *Calcium deficiency* is determined by adding 3 drops of a 1 per cent solution of calcium chloride to 1 c.c. of blood. If coagulation is hastened as compared with a control specimen of blood to which no calcium has been added the test indicates a deficiency of calcium.

(4) *The clot retraction time:* The platelets are intimately concerned in this process which has nothing to do with coagulation of the blood. A prolongation of the clot retraction time will permit abnormal bleeding to occur. In normal blood, retraction of the clot usually begins in an hour or two and is usually complete in from eighteen to twenty-four hours.

c. *Purpura:* Purpura is a symptom common to many diseases in which there is a spontaneous extravasation of blood into or under the skin and mucous membrane. It is not necessarily due to a disturbance in the coagulation of the blood, since it may be the result of abnormalities in the blood vessel walls. Some of the conditions characterized by purpura are purpura hemor-

rhagica, essential thrombocytopenic purpura and hemophilia.

(1) *Purpura hemorrhagica:* This is not a disease but a clinical syndrome which may occur in a number of different diseases. It is characterized by purpura, associated with a marked reduction in blood platelets and a disturbance in blood coagulation.

(2) *Essential thrombocytopenic purpura:* This is a disease entity of unknown etiology. It may be acute or chronic and is characterized by recurring attacks of purpura hemorrhagica.

The blood shows a marked reduction in the number of platelets to below 60,000, with many abnormal forms. There is a post-hemorrhagic secondary anemia and a neutrophilic leukocytosis. The coagulation time is normal. There is a distinct abnormality in the retractility of the clot which is due to the lack of platelets. The bleeding time is greatly prolonged from the normal three minutes to twenty minutes or an hour. A remission is always associated with a rise in the platelet count. During a remission there continues to be a definite reduction in the platelet count but not sufficient to cause purpura. The danger zone for bleeding is 50,000 to 75,000 platelets. Irradiation has been used in the treatment of thrombocytopenic purpura but is not generally regarded as beneficial.

(3) *Hemophilia:* This is a chronic recurring hereditary disease of rare occurrence, characterized by a tendency to bleed as the result of slight injuries. The affection occurs only in males and is transmitted only by females. The condition exists from birth, and bleeding which first occurs at a later age is not due to hemophilia. Recurrent hemorrhages into the joints eventually lead to roentgen appearances which are fairly characteristic for this disease. Such changes are found chiefly in the knee joints.

The blood platelets are normal in number or increased after hemorrhage. The bleeding time is normal and blood clot retracts normally. The principal disturbance is in the coagulation time which is greatly prolonged from one to several hours. A delayed coagulation time up to twenty to twenty-five minutes is not diagnostic of hemophilia since such delay is seen in other conditions.

*B. Blood Chemistry.*

1. *Blood Sugar.*

A determination of the concentration of the sugar in the blood affords a ready means for the clinical detection of various disturbances in carbohydrate metabolism. The *normal blood sugar* value ranges from 80 to 120 mg. per 100 c.c. of blood. Alteration in the blood sugar concentration may occur in one of two directions, either an increase, hyperglycemia, or a decrease, hypoglycemia.

a. *Hyperglycemia:* Diabetes mellitus is by far the most important clinical condition showing a hyperglycemia. The blood sugar value may reach 1,700 mg. per 100 c.c. of blood, but only rarely does it exceed 600 mg. Diabetes is due to a deficiency in the secretion of insulin by the pancreas. This constitutes a state of *hypoinsulinism.* Insulin is essential to the transformation of blood sugar into tissue glycogen. The tissues cannot utilize the sugar of the blood directly for the production of energy. In the absence of sufficient insulin, glucose accumulates in the blood in excessive amounts.

It should be remembered that abnormally high blood sugar values may occur in other conditions than in diabetes. Thus hyperglycemia may be encountered in (1) hyperthyroidism, (2) any condition causing an increased secretion of epinephrin such as pain, various emotions (anger and fear), intracranial disorders as concussion and brain tumor, (3) conditions producing acidosis, such as the acidosis of diabetes, ether and chloroform anesthesia, asphyxia and the acidosis of fever, nephritis and dehydration, (4) conditions characterized by convulsions and strenuous muscular exertion as eclampsia, epilepsy, uremia and tetany.

In any of these conditions, if the glycogen reserve of the liver becomes depleted,

the blood sugar level falls and may actually result in a hypoglycemia. It is for this reason that only 5 to 10 per cent of cases of hyperthroidism show a fasting hyperglycemia and that negative results may occur in any of the conditions named.

Of interest to radiologists is the hyperglycemia which occurs as the result of overactivity in function of the pituitary gland (hyperpituitarism), such as may be encountered in various pituitary disorders (tumor and acromegaly). Pituitrin is antagonistic to insulin and in excessive amounts prevents the transformation of blood sugar into tissue glycogen, permitting a hyperglycemia to occur.

b. *Hypoglycemia:* A low blood sugar concentration is much less frequently observed. It may be encountered in (1) hypothyroidism seen in myxedema and cretinism, (2) hypoadrenalism, as in Addison's disease and extensive burns producing a suprarenal failure, (3) any condition which may cause a depletion of the glycogen reserve of the liver, seen characteristically in acute liver disease (hepatitis) from various causes, less commonly in chronic liver disease such as cirrhosis, syphilis and malignancy, (4) conditions which produce a primary hyperglycemia such as convulsions and muscular exertion may, as the result of depletion of the glycogen reserve, result in hypoglycemia.

A low blood sugar may also occur as the result of hyperinsulinism, either from the therapeutic administration of an excessive amount of insulin or from a hypersecretion of insulin due to hyperplasia or tumors of the pancreas, and in hypopituitarism.

c. *Glucose Tolerance Test:* This test, which is used in the detection of abnormalities of carbohydrate metabolism and which has much the same significance as disturbances in blood sugar concentration, is based upon the principle that a normal individual ingesting a given amount of glucose will show a so-called normal blood sugar curve. This curve consists in an increase in the blood sugar to 140–160 mg. per 100 c.c. of blood within one and a half to two hours and a return to the normal fasting level in two and a half hours.

(1) *Diminished glucose tolerance* is indicated by an abnormally high blood sugar concentration (above 160 mg.) and a prolongation of the hyperglycemia for more than two hours after the glucose ingestion. A diminished glucose tolerance is found in the same conditions in which a fasting hyperglycemia occurs—diabetes, hyperpituitarism, hyperthyroidism, acidosis, etc.

(2) *Increased glucose tolerance* is indicated by little or no elevation of the blood sugar after glucose ingestion and occurs in the same conditions as hypoglycemia, namely, myxedema, cretinism, Addison's disease, hyperinsulinism and hypopituitarism.

d. *Glycosuria:* The presence of glucose in the urine is closely related to abnormalities of blood sugar concentration. It is believed that the kidney possesses a "threshold" for the excretion of glucose. The normal threshold is generally regarded as a blood sugar concentration of 160–180 mg. per 100 c.c. of blood. Not until the blood sugar reaches this level does glucose appear in the urine.

Glycosuria is generally regarded as evidence of diabetes mellitus, and while it is an outstanding feature in this disease, it must be recognized that there are other conditions in which glycosuria may occur. Any condition associated with a fasting hyperglycemia will usually show sugar in the urine when the blood sugar exceeds 160–180 mg. In this connection it is well to remember that glycosuria is not an invariable accompaniment of diabetes even though the blood sugar value may be more than 180 mg. per 100 c.c. of blood. It was formerly thought that under such circumstances functional impairment of the kidneys rendered them incapable of excreting sugar. It is now recognized that in such cases no renal disease exists and the absence of glycosuria is attributed to an elevation of the renal threshold for sugar.

Glycosuria may occur in the absence of a hyperglycemia, as in the following conditions:

(1) *Renal diabetes* (renal glycosuria), a condition in which sugar appears in the urine with a normal blood sugar. It is believed to be due to a lowered renal threshold for glucose. It has no relationship to diabetes mellitus and is apparently harmless.

(2) *Glycosuria of pregnancy*, also thought to be due to a lowering of the renal threshold. It occurs during the latter months in 10–15 per cent of all normal pregnancies.

(3) *Alimentary glycosuria* is a term used to indicate the excretion of glucose in the urine by certain normal individuals after the ingestion of excessive amounts of carbohydrates. The exact cause of this condition is unknown.

(4) Glycosuria occurs in 30–50 per cent of cases of glomerulonephritis, nephrosclerosis and nephrosis and is probably due to a lowering of the renal threshold.

2. *Blood Urea.*

Of the non-protein nitrogen elements of blood, the two of chief interest are urea and uric acid. Urea is the end product of metabolism. This is present normally in the whole blood in a concentration of 12–15 mg. per 100 c.c. of blood. It is usually referred to as blood urea nitrogen, B.U.N. The most important causes of an increase in urea nitrogen are conditions which cause marked suppression of renal function, notably acute and chronic nephritis, urinary obstruction as from prostatic hypertrophy or bilateral urinary calculi, and diminution of functioning kidney tissue as is seen in advanced renal tuberculosis or polycystic disease.

The most important extrarenal cause of an increase in urea nitrogen is acute intestinal obstruction. This is particularly true of obstruction high in the bowel. The exact cause of this effect is not entirely clear. Dehydration and excessive protein destruction due to toxic damage are apparently not chiefly responsible, if they are responsible at all. Recently, Eiman and Karr have emphasized that the rise in urea nitrogen may be an effort on the part of the body to prevent the lowering of plasma osmotic pressure which results from the marked loss of chlorides.

3. *Blood Uric Acid.*

Uric acid is present in the blood in concentrations between 1.5 to 4 mg. per 100 c.c. of blood. While an increase in blood uric acid follows a decreased excretion, such as occurs in nephritis and other renal conditions, the two most notable causes of an increase are gout and leukemia. In gout the rise in blood uric acid is pathognomonic and indicates that the disease is due to a defect in purine metabolism, although the factor of the kidneys' inability to properly excrete this substance is still not entirely ruled out. The absence of uric acid increase in ordinary arthritis serves to distinguish this condition from gout. Since uric acid is derived from the metabolism of tissue nucleoprotein, the increase in uric acid which occurs in leukemia is due to the marked increase in the destruction of cell nuclei which occurs in this disease. Here, too, damage to the kidneys by leukemic infiltration with corresponding inability to excrete uric acid may be important. In determining the response of leukemia to roentgen therapy, frequent determinations of blood and urine uric acid are of value. With the patient on a standard diet, roentgen treatment with consequent increased destruction of circulating cells should result in a marked increase in both the blood and urine uric acid values. The average daily excretion of uric acid in the urine for an adult on a mixed diet is about 0.7 gram.

4. *Blood Calcium.*

The calcium of the blood serum is normally 9–11 mg. per 100 c.c. of blood. The maintenance of this level is chiefly dependent upon the activity of the parathyroid glands, the secretion of which regulates the deposition of calcium salts in the bones and their withdrawal therefrom. Vitamin D plays a somewhat minor rôle in calcium metabolism. Whether the vitamin influences the absorption of calcium from the

intestine or the deposition of it in the bone is not entirely clear.

In *hyperparathyroidism* there is a marked withdrawal of calcium from the bones and a consequent increase of the mineral in the serum, up to 12–20 mg. per 100 c.c. of blood (hypercalcemia). This withdrawal of calcium from bones results in a condition of generalized osteitis fibrosa, which has characteristic clinical and roentgenologic manifestations. Roentgen evidence of a generalized decalcification of the bones without obvious cause should therefore suggest determination of the blood calcium. A great deal of the excess of calcium in hyperparathyroidism is excreted by the kidneys and there is frequently sufficient deposition of lime in these organs to cause stone formation. Occasionally this occurs when the bony changes are still slight or even entirely absent. Blood calcium determinations should therefore be done in cases with multiple renal calculi to rule out the presence of hyperparathyroidism.

A lowering of blood calcium (hypocalcemia) is seen in a number of conditions, particularly in hypoparathyroidism, when the serum calcium falls below 7 mg. per 100 c.c. Symptoms of tetany are usually manifest. Diseases associated with an occasional lowering of blood calcium which have a roentgenological interest are osteomalacia and rickets. There has recently been demonstrated a lowering of blood calcium in both tropical and non-tropical sprue. In these conditions, the defective fat absorption leads to non-absorption of calcium because of the formation of non-soluble salts in the intestine. Snell and Camp have described fairly characteristic roentgen findings in non-tropical sprue, also known as chronic idiopathic steatorrhea or adult celiac disease. The roentgen manifestations include intestinal and skeletal changes. The intestinal appearance varies with the clinical course of the case, so that one may check up on clinical improvement by noting associated evidence of improvement in the roentgen findings in the intestinal tract, as well as by following the blood calcium level. In a typical case one may find delayed gastrointestinal motility, alterations in the mucosal relief of the small intestine, especially of the jejunum, consisting of smoothing of the contours of the lumen, obliteration of the usual markings of the valvulae conniventes, and "clumping up" of the barium in smooth elongated masses. The changes are suggestive of mucosal edema and infiltration of the walls of the small intestine. This portion of the gastrointestinal tract may become somewhat dilated, and the colon begins to assume a smooth contour, with absence of haustrations. As clinical improvement occurs, the roentgen changes noted above begin to regress, and we again see the outlines of the valvulae conniventes. These same changes may occur in any diffuse inflammatory condition of the intestinal tract. Roentgenograms of the skeletal system (1) may be normal (2) may show osteoporosis or (3) we may find evidence of osteomalacia, with marked deformities of the pelvis and pseudofractures.

5. *Blood Phosphorus.*

In many respects the metabolism of inorganic phosphorus is intimately connected with that of calcium. The normal content of inorganic phosphorus in adults ranges from 3 to 4.5 mg. per 100 c.c., in children 4 to 6 mg. Changes are seen in many of the conditions in which there is a change in the serum calcium level.

An increase in serum phosphate, hyperphosphatemia, may occur as the result of excessive doses of vitamin D, hypervitaminosis, administered in the form of cod-liver oil or viosterol. In children this produces a marked increase in density of the zone of temporary calcification at the ends of the long bones. The roentgen appearance may simulate that seen in healing rickets or lead poisoning. In the healing of fractures in adults the serum phosphate may be slightly increased, 5 to 7 mg. per 100 c.c.

Diseases associated with a lowering of serum phosphate, hypophosphatemia, hav-

ing characteristic roentgen findings are rickets, osteomalacia and hyperparathyroidism. In the two former diseases, in which the serum phosphorus may fall as low as 1 to 2 mg. per 100 c.c., the disturbance is due to a vitamin D deficiency. In the earlier stages of hyperparathyroidism the serum phosphorus is also definitely lowered. In the later stages, however, progressive kidney damage decreases the phosphate excretion so that at such a period in the disease the phosphorus may be elevated.

6. *Blood Phosphatase.*

In recent years a great deal of experimental and clinical work has been done upon phosphatase, an enzyme normally present in various tissues of the body. It has the property of hydrolyzing phosphoric acid esters into phosphoric acid and alcohol, and plays an important rôle in the physiology of bone. The *normal value* for serum phosphatase in the adult averages 2.6 units per 100 c.c., the normal range being from 1.5 to 4 units (Bodansky). In children the normal range is much higher, being from 5 to 14 units. This relative increase is true of all young animals and is incident to the active changes of bone formation.

If liver disease with or without jaundice can be excluded, the level of serum phosphatase forms a valuable diagnostic aid in studying diseases of the bone. In bone diseases associated with formation of large amounts of abnormal bone, such as polyostotic Paget's disease, the phosphatase is markedly elevated. The phosphatase is also elevated in the presence of osteoid formation such as occurs in hyperparathyroidism, rickets and osteomalacia. As these diseases heal, the phosphatase level tends to return to normal and this can be used as a test of therapeutic results. The phosphatase values in bone tumors are variable. Metastatic carcinoma of the bone may or may not be associated with elevated phosphatase. There is usually an increase in multiple myeloma, but this is generally not found to be nearly as high as in hyperparathyroidism. This may be of diagnostic value since the roentgen appearance of these two conditions may occasionally resemble each other.

In addition to bone disease, changes in the serum phosphatase are most striking in patients who have obstructive jaundice. Possibly because a great deal of phosphatase is excreted with the bile, common duct obstruction is associated with definite elevation of serum phosphatase, which tends to return to normal when the obstruction is released. When jaundice is nonobstructive in origin, particularly when it is due to severe liver cell damage, the serum phosphatase is either normal or only slightly elevated. These facts have recently been used in differentiating the various types of jaundice. The serum phosphatase is decreased in anemia and in malnutrition.

7. *Blood Cholesterol.*

The total plasma cholesterol ranges from 140 to 200 mg. per 100 c.c. but is usually between 160 to 180 mg. This is composed of two parts, free cholesterol and cholesterol esters, the esters forming 60 to 80 per cent of the total and being largely formed in the liver. The production of cholesterol is not entirely understood, al though it is known to be a product of fat metabolism and that the cells of the reticulo-endothelial system are intimately concerned in its formation. Apparently a fairly normal level is maintained even though no fats are ingested.

Since cholesterol is a lipoid, its increase in the blood constitutes one form of hyperlipemia. Hypercholesteremia is frequently seen in diabetes, the increase paralleling the severity of the disease and explaining, to some extent, the complication of arteriosclerosis which occurs so often. Hypercholesteremia is a regular occurrence in hypothyroidism and since it is rarely seen in other conditions with a low basal metabolic rate, it possesses definite diagnostic value. There is a marked elevation of this lipoid in true nephrosis and the nephrotic stage

of chronic glomerulonephritis. This is looked upon as a compensatory effort to maintain the normal osmotic pressure of the blood which is lowered by protein loss.

Xanthomatosis is a condition dependent upon a state of hyperlipemia. Of roentgenologic interest is the form of xanthomatosis presenting the Schüller-Christian syndrome, cranial defects, exophthalmos and diabetes insipidus. In this condition there is usually a hypercholesteremia and the characteristic granulomatous lipoid masses present consist of large amounts of cholesterol and its esters. This is in contradistinction to the lipoids occurring in two other diseases due to disturbances in fat metabolism, namely lecithin in Gaucher's disease and kerasin in Niemann-Pick's disease.

Since a great deal of cholesterol is excreted in the bile, obstructive jaundice is usually associated with hypercholesteremia. This does not occur in non-obstructive jaundice and if this jaundice is due to severe hepatocellular disturbance, the total blood cholesterol may be lowered. In any case, severe liver disease is usually marked by a decrease in cholesterol (hypocholesteremia), and in some cases the amount may drop to zero. This decrease in cholesterol esters has value as a liver function test in differentiating obstructive from hepatocellular jaundice.

8. *Blood Chlorides.*

The chlorides are among the most important inorganic salts of the body, being widely distributed in all body fluids and tissues. The whole blood normally contains from 450 to 500 mg. of chlorides per 100 c.c. The red cells themselves contain relatively little chloride so that the chloride content of the plasma alone is from 570 to 620 mg. Increase in blood chloride (hyperchloremia) does not occur with great frequency and is of little importance clinically. Decrease in chlorides (hypochloremia) is of fairly frequent occurrence and of considerable clinical significance. One of the most striking causes of hypochloremia is vomiting which results in a loss of chlorides in the gastric secretion. This may be due to the toxemia incident to such conditions as uremia, pyloric stenosis, intestinal obstruction and radiation sickness. The loss of chlorides produces striking changes in body chemistry and may result in a disturbance of the acid-base balance. A lowering of blood chlorides also occurs in various of the acute infections, notably pneumonia, although the exact cause of this is not clear.

Chloride is eliminated chiefly in the urine and the amount excreted in this manner normally approximates the chloride intake. The normal renal threshold value for sodium chloride is 560 to 570 mg. per 100 c.c. of blood plasma. In most instances of hypochloremia there is an associated decrease in urinary chloride. As the concentration of plasma chloride decreases below the threshold value, chlorides may entirely disappear from the urine. The hypochloremia which occurs in nephritis, in the absence of vomiting, is the result of a lowering of the chloride threshold and consequent excessive loss of chlorides in the urine.

9. *Acid-Base Balance.*

The clinical application of the acid-base balance has to do with such common terms as acidosis and alkalosis, which are used so freely by medical men and yet, in many instances, without a clear understanding of the meaning of the terms. The radiologist will encounter these conditions chiefly in his contact with gastrointestinal cases. Thus acidosis may be prominent in patients with severe diarrhea, while alkalosis may result from lesions producing pyloric stenosis and in cases of small intestinal obstruction.

Under normal circumstances the reaction of the blood is very slightly alkaline. The pH of normal blood is very close to 7.4, whereas 7.0 is the pH of neutrality. Even under the influence of markedly diseased states the pH of the blood varies only slightly. In order to maintain this reaction,

despite the influence of various ingested substances and metabolic products, the body possesses certain complicated chemical processes and also means of excreting excessive amounts of acids and alkalies. The chemical protective mechanisms of the body are dependent on the presence in the blood and tissues of buffer systems, so named because of their ability to take up extra amounts of alkalies or acids without changing material in reaction. The most important of these are the bicarbonate and phosphate systems. In addition, the plasma proteins, hemoglobin and chlorides also possess some buffer action. The lungs, kidneys and, to a lesser degree, the gastrointestinal tract, serve to excrete the excess of base or acid. The lungs are chiefly responsible for the excretion of carbon dioxide, the respiratory center being so delicately adjusted that the slightest increase in the acidity of the blood brings about hyperventilation. The kidney is the chief means of excreting the fixed acids. This is accomplished by their excretion as the salts of sodium, potassium, etc., or as ammonium salts. The kidney has the power to manufacture moderate amounts of ammonium when it is necessary to conserve the other bases of the body. The kidney also serves as the most important outlet for the elimination of excessive amounts of base when these are present.

In order to afford a simple conception of the means by which an excessive acidity of the body is prevented, the term "alkali reserve" is given to the total of alkalizing and buffering mechanisms present in the body. Clinically this is usually taken to mean the alkalies present as bicarbonates. Although this version is not strictly accurate, it is sufficiently so for ordinary use.

Measurement of the alkali reserve by determining the carbon dioxide combining power of the plasma serves as a very useful clinical method for determining the acid-base balance. Although it has definite limitations, these are not of great moment in the average case. The carbon dioxide combining power or capacity of the plasma is said to be the number of cubic centimeters of carbon dioxide which can be taken up as bicarbonate by 100 c.c. of plasma under normal atmospheric conditions. This is usually referred to as the plasma $CO_2$ and in adults normally ranges from 50–75 volumes per cent. With *acidosis* the blood loses its ability to take up acid (carbon dioxide is a weak acid) so that the carbon dioxide combining capacity falls. In mild acidosis the reduction is only a slight one. As acidosis becomes more severe the combining power may even be reduced to 10. On the other hand, in alkalosis, larger amounts of carbon dioxide can be bound by the excess alkalies in the blood. The carbon dioxide combining power is increased to 80, 90 or even over 100 volumes per cent.

a. *Acidosis* may be due to the presence of excessive amounts of carbon dioxide, which is relatively unimportant, or a deficiency of alkalies. This last is the responsible factor in such a common condition as diabetic acidosis, in which improper utilization of fats results in the formation of excessive fatty acids which combine with large amounts of base and thus remove them from general use. In advanced kidney disease the inability to excrete acids results in their accumulation in the body with consequent fixation of alkalies. Loss of alkalies as a result of diarrhea may likewise lead to acidosis.

b. *Alkalosis* may also be the result of a number of different causes. It has been noted after deep roentgen therapy and is attributed to a lowering of serum phosphate. It may occur when large amounts of alkalies are fed to individuals whose kidneys are damaged to such an extent that excretion of the excessive base is impossible. In vomiting due to either pyloric stenosis or small bowel obstruction the loss of large amounts of hydrochloric acid leaves behind a great deal of base that accumulates and causes alkalosis to develop.

Alkalosis is a not infrequent complication of pyloric stenosis due to benign ulcer.

The vomiting of large amounts of hydrochloric acid is the most important factor in producing this, but other contributory factors may be alkaline therapy in the presence of associated kidney disease, the loss of blood chlorides as a result of a large hemorrhage, or chloride deprivation because of a long continued salt-poor diet.

The presence of alkalosis may aid very materially in the roentgen interpretation of obstructive lesions occurring at the pylorus. Such lesions are in the vast majority of instances due either to a benign ulcer or malignancy. There are no reliable roentgenologic criteria for making the differentiation. If the patient has an alkalosis the lesion will in most instances be benign. The reason for this is the fact that in most cases of benign ulcer there is a hyperacidity and the loss of chlorides incident to vomiting will produce an alkalosis. In carcinoma, on the other hand, since an achlorhydria is present in the majority of cases, vomiting does not entail the loss of chlorides and thus an alkalosis is not produced.

## II. THE STOMACH

In the clinical investigation of lesions of the stomach much reliance can be placed upon a study of the gastric contents. There are certain pertinent facts regarding the gastric analysis which the radiologist will find of considerable value in his roentgen studies of the gastrointestinal tract.

### *A. Gastric Analysis.*

1. *The Gastric Residuum* (Fasting Stomach): The amount of residuum in the normal fasting stomach ranges from 20 to 100 c.c. This is important for the roentgenologist to keep in mind for one often obtains the impression of the presence of a non-opaque residue as the barium meal enters the stomach. Only when such a residue is in excess of the above figures can it be regarded as of pathological significance. The large non-opaque residues that are frequently present give rise to a characteristic appearance as the barium falls through the fluid content of the stomach. Excessive amounts of gastric residuum may be due to (*a*) hypersecretion, (*b*) retention, and (*c*) regurgitation from the duodenum. The roentgenologist is most commonly interested in the lesions producing retention such as carcinoma of the pylorus or stenosing peptic ulcer of the pylorus or duodenum.

2. *Color:* The normal gastric juice is colorless. The most significant change in color is the bright or dark red, brown, or black due to the presence of blood which may occur in a variety of conditions such as carcinoma and chronic passive congestion of the stomach, portal cirrhosis, peptic ulcer, gastric lues, acute gastritis and hemorrhagic blood dyscrasias. The report of blood in the gastric contents should prepare the roentgenologist for an organic lesion of the stomach but he should not always expect to find such pathology in view of the multiplicity of conditions outside the stomach which may be responsible for the presence of blood. The time honored "coffee grounds" appearance associated with carcinoma of the stomach is due to the fact that the blood escaping from a carcinoma usually coagulates and it is the disintegration of such a clot which gives rise to the "coffee grounds" appearance.

It is interesting to note that the gastric residuum is either yellow or green in 55 per cent of normal individuals and that in about 25 per cent this is accounted for by the regurgitation of bile from the duodenum. Roentgenologically one occasionally obtains the impression that barium is passing back into the stomach from the duodenum. This need cause little concern when one considers the above figures.

3. *Gastric Acidity:* Of prime importance in the study of the gastric contents is the amount and kind of acid present. The acidity depends upon the presence of free hydrochloric acid, hydrochloric acid combined with protein and acid salts and certain organic acids. All taken together constitute the total acidity which in the gastric residuum normally ranges from 10 to 50. These figures refer to the number of

cubic centimeters of tenth normal sodium hydroxide required to neutralize 100 c.c. of gastric contents. The normal range of free hydrochloric acid in the gastric residuum is from 0 to 30. The organic acids are lactic and butyric. They are not generally regarded as being present normally in the gastric contents and usually are found in cases of gastric retention, especially carcinoma.

In addition to the determination of the acidity of the gastric residuum much valuable information is to be obtained by

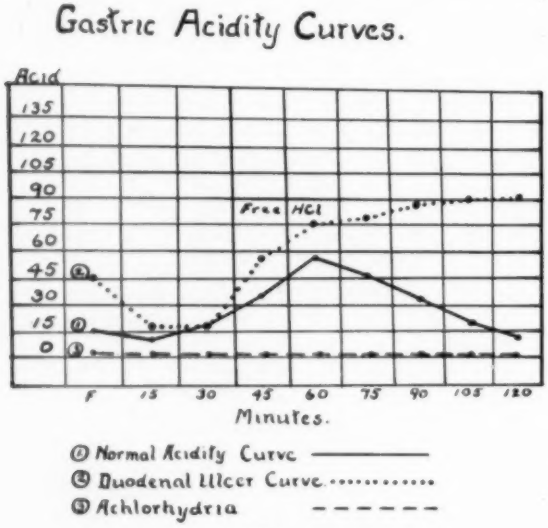


Fig. 2

means of *fractional gastric analysis*, which is a study of the manner in which the stomach responds to stimulation. Various test meals such as those devised by Ewald, Boas and Riegel are used to stimulate gastric secretion. Of more recent development and of considerable value is stimulation with histamin. This substance when injected subcutaneously acts as a powerful stimulant to gastric secretion and will thus cause hydrochloric acid to be secreted when such acid is absent by other stimulants. It thus serves to differentiate a true from a false achylia.

In fractional gastric analysis, after the administration of the test meal, 10 c.c. of the gastric contents are aspirated every fifteen minutes for two to three hours. Each specimen is examined for its degree of acidity and both the free hydrochloric acid and total acidity are charted. This constitutes what is known as the *acidity curve*. Fractional gastric analysis affords accurate information concerning gastric digestion and the motor activity of the stomach.

While the determination of gastric acidity is of considerable clinical importance it must be recognized that there is much variation in health and many exceptions to what may be anticipated in disease. There also exists among the workers in this field considerable difference of opinion regarding the diagnostic value and significance of certain acidity curves. The roentgenologist will find of value, therefore, only those facts regarding which there is little dispute. Thus the *normal acidity curve* (Fig. 2) is one in which the free HCl rises sharply and reaches its maximum of 40 to 50 at the end of the first hour and returns to the fasting level at the end of the second hour. The curve of total acidity parallels that of free HCl, usually reaching a maximum of 60 to 70. Such a curve will usually exclude an organic lesion of the stomach or duodenum except a gastritis for which there is no typical acidity curve. The *second curve* which is sufficiently constant and characteristic to be of practical value is the one found in duodenal ulcer. This curve rises sharply during the first hour, the free HCl reaching a high level of 80 to 90. This is maintained and may even go higher during the second hour and is often continued into the third hour after the test meal. This type of hyperacidity is found in 70 to 80 per cent of cases of duodenal ulcer. It is also found in duodenitis and is therefore of no value in the differential diagnosis of these two conditions which may simulate each other both clinically and roentgenologically. A very high acidity with ulcer is usually indicative of a bad prognosis. A somewhat similar curve but one which does not reach as high a level is sometimes seen in extragastric lesions such as cholecystitis or chronic appendicitis. It is referred to as an *extragastric curve*. The *third curve* of

practical value is the one denoting an *achlorhydria* and especially if there is also an absence of enzymes (*achylia* or *achylia gastrica*). This type of acidity prevails in 60–80 per cent of cases of gastric carcinoma. An outstanding condition in which achylia gastrica is almost an invariable accompaniment is pernicious anemia. A true achylia can be detected by means of a subcutaneous injection of histamin, whereby neither free HCl or gastric enzymes appear in the gastric contents.

*Hypoacidity* prevails when the acid figures are below those established as normal. Hypoacidity is of little practical value since about 25 per cent of apparently normal individuals fall in this group and is found in such a wide range of unrelated conditions from chronic constipation to hyperthyroidism. Age is also an important consideration in hypoacidity since it is usually found in children and in elderly individuals. The high acidity of middle life falls progressively with advancing years so that an achlorhydria is not uncommon during old age. This may be the result of a physiological atrophic gastritis.

It must be borne in mind that the gastric analysis like the roentgen examination becomes significant only when correlated with the rest of the clinical picture. To the roentgenologist a knowledge of the gastric acidity is of particular value in those cases of frequent occurrence in which the roentgen findings are those of gastric ulcer. It is, in many instances, difficult to determine whether the lesion represents a benign or malignant ulceration. According to Bockus, in carcinoma of the stomach there will be an achlorhydria in 80 per cent of cases, hypochlorhydria in 10 per cent and a normal acidity in 10 per cent. This knowledge should be of considerable aid in determining the nature of gastric defects observed roentgenologically. One should hesitate to make a diagnosis of benign ulcer in the presence of an achlorhydria.

The state of gastric acidity is of further value to the roentgenologist in its relation to gastric motility. In *achylia* and *achlorhydria* there is a rapid outpouring of the barium meal from the stomach. This is a fairly constant phenomenon that has been amply verified in the experience of most roentgenologists. In any case of gastric hypermotility it is well to know whether the patient has an absence of free HCl. *Hyperacidity*, on the other hand, produces a delay in gastric evacuation. This fact is not so readily appreciated by the ordinary roentgen examination since the six hour limit for gastric clearance, that is almost universally accepted as normal, does not take into account the wide range of gastric evacuation incident to varying degrees of hyperacidity.

4. *Gastric motility* as determined clinically depends upon the time required for the stomach to empty itself after an Ewald or Boas meal. The average time is about two hours, with normal variations, ranging from one and a half to two and a half hours. We have frequently noted a discrepancy between the clinical and the roentgenological determinations of gastric evacuation. Whereas a delay in gastric clearance has been reported by the test meal, the emptying time of the stomach has been clearly within normal limits according to roentgenologic standards. Obviously the reason for this is the fact that the time limit for gastric clearance varies considerably in the two methods, two and a half hours by gastric analysis and six hours roentgenologically. There is no doubt that the clinical determination of gastric motility is much more precise and accurate and certainly more physiological than the barium meal method. In cases under observation with quiescent gastric or duodenal lesions, a relapse has frequently been predicted, even before the onset of symptoms, by an increase in emptying time of the stomach as determined by gastric analysis and long before any delay in gastric motility is detectable by the ordinary roentgen examination. Also, when such lesions are healing, evidence of gastric retention by gastric analysis will remain long after such signs have disappeared by the barium meal

method. In functional disturbances of the upper gastrointestinal tract, alterations in gastric motility are readily detected by gastric analysis, whereas a six hour barium residue is nearly always the result of some organic lesion.

*B. Gastric Microscopy.*

The microscopic examination of the stomach contents reveals certain facts that are of value in the study of gastric lesions. Evidence of gross or microscopic food in the fasting residuum is a manifestation of delayed emptying of the stomach, while after an Ewald meal, over 15 c.c. of food and more than 30 c.c. of fluid at the end of two hours has the same significance. Small amounts of microscopic food probably indicate retention in rugal folds when the bulk of the test meal empties normally. This is probably due to unusually deep rugae or excessive amounts of mucus to which food particles tend to adhere.

Gastric microscopy finds its greatest value in the study of gastritis, a condition which, in recent years, has regained some of its former popularity. This renaissance has been due, in no small measure, to the recent intensive roentgenological studies of the gastric mucosa, and now with direct visualization of the interior of the stomach made possible by the gastroscope, gastritis bids fair to become again the gastroenterologist's chief stock in trade. Evidence of gastritis as determined by the microscopic study of the stomach contents is manifested by the finding of (*a*) exfoliated gastric cells or strips of gastric mucosa, (*b*) a great excess of mucus, (*c*) phagocytic cells mixed with gastric cells and (*d*) an excess of red blood cells when not due to trauma. As has already been mentioned there is no typical acidity curve indicative of gastritis; however, an achylia with microscopic evidence of gastritis is suggestive of an atrophic variety of this condition. A microscopic study of the gastric contents gives no aid in the detection of peptic ulcer. This must usually be left to the roentgenologist. In the presence of ulcer, whether gastric or duodenal, there is almost invariably a gastritis. This is quite readily verified roentgenologically.

III. THE LIVER

While the study of liver function is not ordinarily of direct interest to the roentgenologist, the use of the simpler tests may be of great assistance to him in an occasional case. Determination of liver function presents great difficulty, since this organ has tremendous reserve capacity and powers of regeneration and has such a multiplicity of functions that the value of any single test is definitely limited. At the present time there is no liver function test, which, if negative, can be said to entirely rule out the presence of advanced hepatic disease. There are many tests, however, to which positive responses definitely indicate liver dysfunction. The combined use of these methods of study is of great diagnostic value.

Of the procedures now in use, those which enjoy the most widespread application are studies of jaundice and of bilirubin metabolism by such means as the van den Bergh reaction and the examination of the urine for urobilinogen, excretory tests such as the bromsulphalein test and determinations of metabolic activity, an example of which is the galactose tolerance test.

*A. Jaundice.*

*Jaundice* or *icterus* is one of the important clinical manifestations of gallbladder and liver disease, although it may occur in other conditions. The yellow color found in the skin and conjunctivae which constitutes clinical jaundice is the result of the presence in the tissues of bilirubin. Bilirubin is the chief pigment of human bile and is derived from the disintegration of the hemoglobin of the blood. Researches in recent years have fairly well established the fact that the reticulo-endothelial cells of the bone marrow, spleen and liver are responsible for the transformation of the hemoglobin into bilirubin and other bile

pigments. The polygonal cells of the liver withdraw bilirubin from the blood and excrete it in the bile. Any disturbance in the formation and excretion of bilirubin may give rise to excessive amounts of bilirubin in the circulating blood, a condition known as hyperbilirubinemia. The normal amount of bilirubin in the blood ranges up to 0.4 mg. per 100 c.c. of blood, but is usually less than 0.2 mg. When the amount of bilirubin in the blood is in excess of normal yet not sufficient to discolor the tissues as seen in the skin and conjunctivae, the condition is termed latent jaundice. It has been shown that the concentration of bilirubin may be increased three to four times before evidence of jaundice appears in the tissues.

The most frequently used classification of jaundice is as follows:

(1) *Hemolytic Jaundice:* This relatively rare type of jaundice is the result of excessive red blood cell destruction and consequent formation of more bilirubin than the liver cells can excrete. There is some question as to whether anoxemia of the liver cells may not play a part in the production of the jaundice. The typical example of this type of jaundice is the disease known as congenital hemolytic jaundice, although occasionally hemolytic poisons cause it.

(2) *Hepatocellular Jaundice:* This results from such marked disturbance of liver cell function that bilirubin excretion does not take place. This is frequently seen as a result of toxic damage to the liver from such poisons as cinchophen and the arsenicals. In the majority of cases of so-called catarrhal jaundice the underlying process is hepatocellular damage.

(3) *Obstructive Jaundice:* This is produced by mechanical obstruction of the biliary passages, such as may be caused by common duct stone or carcinoma of the head of the pancreas. As a result of the obstruction bile excretion is impossible so that a return of bilirubin to the blood stream occurs.

*B. Liver Function Tests.*

1. *Van den Bergh Reaction.* Of the means which are used to determine the amount of bilirubin in the blood, the most reliable is the van den Bergh reaction. This depends upon the production of a characteristic color when Ehrlich's diazo reagent is brought into contact with bilirubin. The normal range of bilirubin in the blood as indicated by the van den Bergh reaction is 0.2 to 0.4 mg. per 100 c.c. It was at first thought that this test would be a means of differentiation between obstructive and hepatocellular jaundice. It is now known that the test is incapable of making this differentiation, so that, although it will differentiate the hemolytic from the nonhemolytic types of icterus, it does not have the great diagnostic value which was formerly attributed to it. It is of great use, however, in measuring the amount of bilirubin in the blood stream, particularly in determining amounts of excessive bilirubin so small as not to cause clinical jaundice.

2. *Determination of Urobilinogen in the Urine.* One of the most delicate of the liver function tests now in use is the examination of the urine for urobilinogen. Upon entering the intestines bilirubin is converted by a process of putrefaction into urobilinogen. This is then oxidized into urobilin. Although the bulk of the urobilin is excreted in the feces, a fairly large amount is reabsorbed through the portal circulation and carried back to the liver. Here, the major portion of the reabsorbed urobilin is reconverted into bilirubin and hemoglobin. Urobilin normally occurs only in the feces and not in the urine; urobilinogen, on the other hand, is present in small amounts in both bile and urine. Examination of the urine for urobilinogen is of value in diagnosis of liver disease, for when there is liver cell damage, increased amounts are found in the urine. The only precaution to be observed is the necessity for ruling out the presence of one of the hemolytic conditions. These are associated with an excessive pigment metabolism which may also cause large amounts of urobilinogen to be

present in the urine. In the absence of any pathological hemolysis, however, increased urobilinogenuria is indicative of hepatic disease.

The absence of urobilinogen from the urine is an equally important diagnostic aid. The only possible cause for continued absence of this substance in the urine is an obstruction of bile flow. Therefore, in the presence of jaundice examination for urobilinogen is of value in determining whether or not the jaundice is obstructive in origin. Long-standing absence of urobilinogen is highly suggestive of the jaundice being due to some malignant process.

As ordinarily performed, the examination for urobilinogen is very simple. It consists merely in determining to what dilution the reddish color, obtained by mixing Ehrlich's aldehyde reagent and urobilinogen-containing urine, persists. Normally the color is present in urine diluted to about 1 to 20. In the presence of severe liver damage it may be necessary to dilute the urine up to 1 to 200 or even more before reaching the end point.

3. *Bromsulphalein Test.* Of the various dye substances which have been used to test liver function, the one which is now most generally utilized is bromsulphalein. This dye is, under normal conditions, almost entirely excreted by the liver cells into the bile. Only under the circumstance of marked liver cell disease is any appreciable amount excreted by the kidneys.

In the test, as generally performed, the patient is given an intravenous injection of 2 mg. of dye per kilo of body weight. A specimen of blood is taken in half an hour. By a simple colorimetric process it is very easy to determine the content of dye in this specimen. Normally there should be no dye in the thirty minute specimen. In the presence of liver disease, the amount of dye retention may be as high as 70 per cent. Occasionally a 5 mg. per kilo dose is used. If this is given it must be remembered that even a normal person may have a 10 per cent retention at thirty minutes. In the absence of jaundice, bromsulphalein retention may be considered quite definite evidence that there is severe liver damage. This may be of a cirrhotic nature or due to such conditions as congestive heart failure or metastatic carcinoma. Since it requires fairly marked liver damage to produce dye retention, a positive bromsulphalein test in a non-jaundiced patient is of serious import. In the presence of jaundice, this test is of little value. The dye being excreted in the bile, it is quite obvious that if the bile does not pass, dye excretion is impossible. In the patient with jaundice, therefore, it is impossible to state whether dye retention is the result of liver cell disease or of obstruction to bile flow.

It has been assumed that a high degree of bromsuphalein retention would indicate that dyes used for gallbladder visualization in cholecystography would not be excreted by the liver in sufficient quantities and that failure to demonstrate the gallbladder might thus be due to liver dysfunction rather than gallbladder disease. This point is still not entirely settled. It is possible, however, that even in the presence of a diseased liver, gallbladder visualization may take place, since even a damaged liver may slowly excrete a sufficient amount of the dye to be concentrated by the gallbladder. There is definite reason to believe, however, that in the presence of jaundice or of evidence of liver cell damage, cholecystography is better omitted in order to avoid further hepatic injury.

4. *Galactose Tolerance Test.* It has been found that the galactose tolerance test offers a means of differentiating the jaundice due to disease of the liver cells (hepatocellular jaundice) from that due to obstruction of the bile ducts (obstructive jaundice) or hemolysis. In this respect it is of great value, since, although there are other means of making such a differentiation, they are somewhat difficult of application.

While there are many modifications of the test the following method has given satisfactory results: The patient is given

40 grams of galactose orally. All the urine is collected for the next five hours. The amount of galactose contained in this specimen of urine is determined. The interpretation of the test is as follows:

(1) An excretion of 2 grams or less of galactose is normal.

(2) An excretion of between 2 and 3 grams is weakly positive and is suggestive of liver disease.

(3) More than 3 grams of galactose in the urine is positive and is a definite indication of liver cell disease.

Tumen and Piersol found a positive reaction in 54 per cent of cases of toxic hepatitis and in 78.3 per cent of cases of catarrhal jaundice, while in obstructive jaundice a positive reaction was obtained in only 5.5 per cent of cases, thus indicating the value of alimentary galactosuria in differentiating jaundice due to actual liver disease from that of biliary obstruction.

Circumstances which detract from the value of the galactose tolerance test are the frequency with which negative results are obtained in cases of undoubted liver disease and the fact that the test is usually negative if the hepatitis if of long standing. The cause assigned for the negative results in the latter instance is the belief that liver regeneration sufficient to carry on normal galactose metabolism may occur in chronic hepatitis. Tumen and Piersol summarize the value of the galactose tolerance test in the following statement: "We feel that a positive galactose tolerance test in jaundice is almost pathognomonic of hepatocellular damage. If the test is negative, this condition is not ruled out, particularly if the test is carried out late in the course of the illness."

## IV. THE GALLBLADDER

### *A. Biliary Drainage.*

The examination of the bile procured by duodenal intubation has proved of great value in the diagnosis of biliary disease, particularly of gallstones. The fundamental principle of this procedure is the relaxation of the sphincter of Oddi induced by the introduction of various substances, notably magnesium sulphate solution into the duodenum. The actual technique of duodenal drainage is not difficult. It affords an accurate picture of gallbladder function and enables one to detect the presence of stones. In the patient with a normal gallbladder, there is usually secured from 50 to 75 c.c. of very dark, concentrated bile which is now known to come directly from the gallbladder. This is the so-called B bile. The absence of this concentrated bile on repeated drainages can be accepted as good evidence that the gallbladder is not functioning well enough to concentrate bile or that the cystic duct is occluded. If on repeated drainages only small amounts of B bile are obtained, it may usually be assumed that the gallbladder has retained only a fraction of its concentrating power, or that it has lost this function entirely and that some branches of the biliary ducts have developed the ability to concentrate bile. The macroscopic examination of the bile is therefore of aid in evaluating gallbladder function.

The most important elements to be searched for with the microscope are the flat, clear, sharply defined, rectangular crystals of cholesterol and the brilliant, golden yellow or orange pigment which is assumed to be calcium bilirubinate, although its true chemical nature is not yet entirely proved. If both these elements are found together in the bile it may be stated with almost 100 per cent certainty that gallstones are present. Stones are present in approximately 90 per cent of those patients whose bile contains either calcium bilirubinate pigment or cholesterol crystals alone. When cholesterol crystals only are found repeatedly, the condition known as cholesterosis of the gallbladder may be present, a condition frequently referred to as the "strawberry" gallbladder. Occasionally calcium bilirubinate pigment is present alone in the bile of patients who have chronic obstructive jaundice without stones.

It is thus seen that the microscopic ex-

amination of the bile is of considerable importance in the diagnosis of gallstones. Bockus and his coworkers reported a series of 148 patients studied preoperatively by drainage or cholecystography in whom operation or autopsy subsequently proved the presence of gallstones. Drainage was performed in 143 of these cases and revealed evidence of gallstones in 83.2 per cent. It is necessary to emphasize that this degree of accuracy was reached by repeated studies. In many instances there was no evidence of stone on the first drainage, and if the first drainages had been relied upon, the percentage of positive diagnoses would have been reduced to 59.3 per cent. Repeated drainages are particularly necessary in those cases with little or no B bile because the elements diagnostic of cholelithiasis are usually found in the concentrated gallbladder bile.

It should not be felt that gallbladder drainage and cholecystography are antagonistic methods of study but rather that they supplement each other. Whenever cholecystography or drainage reveals positive evidence of gallstones no further diagnostic procedure is necessary. Drainage is particularly valuable in the study of those patients whose gallbladders are visualized poorly or not at all by cholecystography. In such cases, drainages may make a definite diagnosis of stone, or by repeatedly failing to demonstrate concentration of bile, confirm the presence of a nonfunctioning gallbladder, which usually means stone. On the other hand, in an occasional case of cystic duct block it may be impossible to find evidence of cholelithiasis in the bile but roentgen examination may definitely show stones.

Microscopy of the duodenal contents gives information of inflammatory processes involving the duodenum, such as a duodenitis, in much the same manner as a gastritis may be diagnosed by a microscopic study of the gastric contents. The findings are essentially the same with the exception of the presence of duodenal cells rather than cells from the stomach.

## V. THE KIDNEYS

### *A. Tests of Renal Function.*

The renal function tests which now enjoy the widest use are the phenolsulphonphthalein test which was originally introduced by Rowntree and Geraghty in 1912, a simultaneous study of the urea of the blood and urine, usually by means of the urea clearance test of Van Slyke, and the determination of the kidney's ability to form urine of high specific gravity by a concentration test such as those suggested by Addis or Fishberg.

1. *Phenolsulphonphthalein Test.* The principle and technique of the phenolsulphonphthalein test are so familiar as to require no repetition here. The test is frequently referred to as the P.S.P. Normally 40 to 50 per cent of the dye should be eliminated during the first hour and 20 to 35 per cent the second hour, with a total of 60 to 75 per cent for the two hours. At present, it is realized that there are factors which limit the value of this test. Thus, if there is edema, even though this is not due to renal disease, the prerenal deviation of fluid will cause a lowering of the amount of dye passed. Low figures are, therefore, frequently obtained in cases with non-renal edema. On the other hand, the test may give normal results in individuals with advanced but well compensated kidney disease, in whom, with the passing of large amounts of urine of low specific gravity, normal amounts of dye may be excreted.

2. *Urea Clearance Test.* The urea clearance test of Van Slyke gives an accurate means of measuring the ability of the kidneys to excrete this substance. After an ordinary breakfast without tea or coffee, two specimens of urine are collected at the end of two periods of exactly one hour each. Blood for determination of urea nitrogen is taken. Knowing the urea nitrogen of the blood and urine and the volume of the urine per minute, it is possible to determine the volume of the blood cleared of urea per minute. This may be expressed in cubic centimeters or percentage of normal. Re-

cently the latter method of reporting has been used. The chief technical difficulty with the test has been the necessity of having patients completely empty the bladder at exactly hourly intervals. This difficulty is particularly evident in hospital wards.

It is now felt that the urea clearance test gives an extremely accurate index of renal function. Abnormal readings are obtained with a degree of renal damage which might otherwise go unrecognized. The test affords accurate information that is valuable not only diagnostically but also prognostically. Repeated use in acute nephritis aids in determining which cases will go on to chronic disease. The relative lack of delicacy of mere determination of blood urea nitrogen is revealed by the fact that the urea clearance must be reduced to 20 per cent of normal before urea begins to accumulate in the blood.

3. *Fishberg Concentration Test.* The simplest method of studying the functional ability of the kidneys is by a concentration test such as that of Fishberg. This consists merely in noting the specific gravity of three hourly specimens of urine obtained in the morning after a relatively dry but high protein evening meal. The specific gravity of at least one specimen should exceed 1.025. With advancing kidney impairment the specific gravity drops, finally approaching 1.010. The only inaccuracy of this test occurs in individuals who are in the stage of recovery from edema, at which time low specific gravity urine may be passed even by those with normal kidneys. Otherwise, the ability of the kidney to concentrate urine can be easily measured by this very simple means, as impaired renal function can be diagnosed, even if it is well compensated.

To the roentgenologist, renal function is of particular importance in connection with excretory urography. Inasmuch as visualization of the urinary tract by this procedure is dependent upon the ability of the kidneys to excrete an opaque dye given intravenously, the amount and rapidity of dye excretion is directly proportionate to the state of renal function. The clinician frequently loses sight of this fact in requesting an examination of the urinary tract by excretory urography for a patient whose renal function is markedly impaired. Such an examination is a complete waste of time and material. In any questionable case the roentgenologist does well to inquire as to the functional capacity of the kidneys before proceeding with the examination. Furthermore, when poor visualization is obtained in excretory urography one should always determine whether this is due to impaired renal function before attempting to interpret the urogram. A simple P.S.P. determination, phenolsulphonphthalein elimination, will give sufficiently accurate information for the purpose of excretory urography. While we do not know precisely the degree of kidney damage required for non-visualization to occur, our experience would seem to indicate that when renal function is less than 25 per cent of normal, no visualization will be obtained by excretory urography.

*B. Bence-Jones Protein.*

This is a peculiar albuminous substance which may be found in the urine frequently, but not exclusively, in cases of multiple myeloma. It differs from all other substances in that a precipitate resembling curdled milk appears when acid urine containing this protein is heated to 50 or 60° C. This precipitate redissolves on boiling. As the urine is allowed to cool, the precipitate or coagulum again appears.

In all cases of obscure bone pain, and in all cases of obscure anemia, the urine should be investigated for the presence of Bence-Jones protein. According to Geschickter and Copeland, it is present in the urine in 65 per cent of cases of multiple myeloma. It may appear in the urine before any bone marrow lesions can be demonstrated, and it may disappear from the urine at a time when there is extensive evidence of the myelomatous lesions in the

bone marrow. It has been reported in cases of metastatic carcinoma involving the osseous system, in myelogenic osteosarcoma, in osteomalacia, and in lymphatic leukemia. It is therefore not pathognomonic for multiple myeloma.

### SUMMARY OF NORMAL VALUES

I. THE BLOOD

A. Cellular elements of the blood

1. Red blood cells (erythrocytes)
   a. Number—Males, 4,500,000 to 6,000,000 per cubic mm. of blood.
      Females, 4,000,000 to 5,500,000 per cubic mm. of blood.
   b. Reticulocytes—Less than 1 per cent of the red blood cell count.
2. Hemoglobin
   Males—14 to 18 grams (84 to 108%) per 100 c.c. of blood.
   Females—12 to 15.5 grams (72 to 93%) per 100 c.c. of blood.
3. Volume index
   0.85 to 1.0
4. Color index
   0.85 to 1.0
5. Sedimentation rate
   3 to 5 mm. (upper normal limit—10 mm.)
6. Fragility test
   a. Hemolysis begins at 0.44 per cent concentration of salt solution.
   b. Hemolysis complete at 0.34 per cent concentration of salt solution.
7. White blood cells
   a. Total number per cubic mm. of blood—5,000 to 10,000.
      (1) Leukocytes—Normal Range

| | 3 MONTHS TO 3 YEARS | 3 TO 5 YEARS | OVER 5 YEARS AND ADULTS |
|---|---|---|---|
| Neutrophiles | 2000–7000 | 3000–8000 | 3000–7000 |
| Basophiles | 0–50 | 0–50 | 0–50 |
| Eosinophiles | 25–700 | 50–700 | 50–400 |
| Lymphocytes | 4000–9000 | 2500–6000 | 1000–3000 |
| Monocytes | 25–700 | 25–700 | 100–600 |

   b. Nuclear index
      (1) Normal findings—15, or over.
      (2) Slight shift to the left—10 to 15.
      (3) Moderate shift to the left—5 to 10.
      (4) Marked shift to the left—Under 5.
8. Blood platelets (thrombocytes)
   200,000 to 400,000 per cubic mm.
9. Bleeding time
   3 minutes, or less.
10. Coagulation time
    2 to 12 minutes, depending upon method used.
11. Clot retraction time
    a. Begins in 1 to 2 hours.
    b. Complete in 18 to 24 hours.

B. Blood chemistry

1. Blood sugar
   a. Normal values—80 to 120 mg. per 100 c.c. of blood.
   b. Glucose tolerance test
      (1) Normal blood sugar curves
         Within 1st hour—
            Blood sugar increases to 140–160 mg. per 100 c.c. of blood.
         Within 1½ to 2 hours—
            Blood sugar decreases to 120 mg. per 100 c.c. of blood.
         Within 2½ hours—
            Blood sugar decreases to normal fasting level.
   c. Normal kidney threshold of blood sugar concentration 160 to 180 mg. per 100 c.c. of blood.
2. Blood urea nitrogen
   12 to 15 mg. per 100 c.c. of blood.
3. Uric acid
   a. Normal values in blood—
      1.5 to 4 mg. per 100 c.c. of blood.
   b. Normal values for daily excretion in urine for an adult on a mixed diet—
      0.7 grams.
4. Blood calcium
   9 to 11 mg. per 100 c.c. of blood.
5. Blood phosphorus
   a. In adults—3.0 to 4.5 mg. per 100 c.c. of blood.
   b. In children—4.0 to 6.0 mg. per 100 c.c. of blood.
6. Blood phosphatase
   a. In adults—1.5 to 4.0 units per 100 c.c. of blood (Bodansky).
   b. In children—5.0 to 14 units per 100 c.c. of blood (Bodansky).
7. Blood cholesterol
   140 to 200 mg. per 100 c.c. of blood.
8. Blood chlorides
   a. Blood plasma chlorides—
      570–620 mg. per 100 c.c. of blood plasma.
   b. Normal renal threshold value for sodium chloride—
      560–570 mg. per 100 c.c. of blood.
9. The acid-base balance
   a. Plasma $CO_2$—50 to 75 volumes per cent.

II. THE STOMACH
- A. Gastric analysis
  - 1. Fasting stomach
    - a. Gastric residuum—20 to 100 c.c.
    - b. Total Acid— 10 to 50.
    - c. Free hydrochloric acid— 0 to 30.
  - 2. After test meal
    - a. Normal acidity curve
      - (1) At end of 1st hour free hydrochloric acid reaches maximum of 40 to 50.
      - (2) At end of 2nd hour free hydrochloric acid returns to the fasting level.
      - (3) Curve of total acidity—parallels curve of free hydrochloric acid; usually reaches maximum of 60 to 70.
  - 3. Normal emptying time of stomach
    - a. After test meal—1½ to 2½ hours.

III. THE LIVER
- A. Liver function tests
  - 1. Normal amount of bilirubin in blood (van den Bergh reaction)
    Less than 0.2 mg. up to 0.4 mg. per 100 c.c. of blood.
  - 2. Urobilinogen in urine (Ehrlich's aldehyde reagent)
    Color reaction up to 1 to 20 dilution.
  - 3. Bromsulphalein test
    No retention of dye in blood 30 minutes after injection.
  - 4. Galactose tolerance test (after ingestion of 40 grams of galactose)
    - a. Galactose excreted in 5 hour urine specimen—2 grams, or less.

IV. THE GALLBLADDER
- A. Biliary drainage
  - 1. 50 to 75 c.c. of B bile.

V. THE KIDNEYS
- A. Tests of renal function
  - 1. Phenolsulphonphthalein test (P.S.P.)
    - a. Amount of dye eliminated
      - (1) During the first hour—40 to 50%.
      - (2) During the second hour—20 to 35%.
      - (3) Total for two hours—60 to 85%.
  - 2. Urea clearance tests
    - a. Standard blood urea clearance (urine volume output 2 c.c., or less, per minute)—54 c.c.
    - b. Maximum blood urea clearance (urine volume output greater than 2 c.c. per minute)—75 c.c.
  - 3. Fishberg concentration test
    - a. Specific gravity of at least one of the 3 hourly specimens—above 1.025.

We are greatly indebted to members of the staff of the Graduate Hospital for the aid so generously given in the preparation of this paper.

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## DISCUSSION

Dr. Frank W. Konzelmann, Philadelphia. What Dr. Kornblum has said might apply to the clinical pathologist as well as to the radiologist. He might have entitled his paper, "What the Clinical Pathologist Ought to Know About Clinical Pathology."

I had the good fortune to read this paper before it was presented and in it there are many very, very important points that time did not permit him to present here.

Dr. Edward Chamberlain at Temple Uni-

versity has shown this same interest in clinical pathology that Dr. Kornblum speaks of. I assure you it has meant much to me to have the aid and the cooperation of the radiologist in my work as it must have meant to Dr. Chamberlain in knowing something of the problems of the clinical pathologist. By our teamwork, we have both learned more about the patient, and the patient has benefited through greater accuracy of diagnosis.

In order to make the basis of clinical pathology more easily understood by not only the clinician but the radiologist and the surgeon, we have hit on the plan of putting the accepted range of normals on the chart where the laboratory findings are recorded.

(Slide) This is the type of blood chart that is used at Temple University Hospital. You will note we have no standard normal for hemoglobin. It is reported in grams per 100 c.c. of blood. The gram value per 100 c.c. varies with the age and sex. Dr. Kornblum did not have an opportunity to speak of the importance of this point, yet I wish he had. If one stops to consider for just a moment how hemoglobin is often reported, one can easily see how confusing the results might be. If we continued to use the old system of percentage values, there would be no comparison of the values of hemoglobin in different institutions. The 100 per cent value on each of the commonly used hemoglobinometers is different. If we employ gram values and in a given case know the relation of the gram value to the normal for that age, it is easy to estimate the percentage of the normal (for adults, multiply the gram value by 6). For instance, in this case, 7 grams was the example I used. Multiply 7 by 6, obtaining 42 per cent, which is the percentage of average normal for this hypothetical case.

Children have higher hemoglobin values than adults. The child at birth has a hemoglobin value of 23 grams; at one year, 12 grams; at fifteen years, 15 grams; and at the age of twenty to sixty, it is 16.9 per 100 c.c. of blood. No 100 per cent value can be uniformly or sensibly applied to such a wide range of figures.

Another point which Dr. Kornblum did mention was the importance of reporting the various leukocytes in total numbers per cubic millimeters of blood. On our charts, the neutrophile range is from 3,000 to 7,000 and the lymphocyte from 1,000 to 3,000. So frequently a clinician will, after receiving repeated eosinophile counts of 10 per cent or more in a certain count, request a stool examination for ova or parasites. If none are found, he will ask, "Isn't it strange, with an eosinophile count of 10 per cent, would not one expect parasitic infestation?" My answer is, "No, because the total white count was but 5,000. Ten per cent of 5,000 is 500, a figure within the normal range." On the other hand, a patient with 15,000 total count and a 6 to 7 per cent eosinophile count will have a true eosinophilia, 1,050 per c.mm., yet the number per cent is but slightly above that given as normal (4–6 per cent). If one reports the cells in absolute values and one has the normal range on the chart, it is easy for the clinician, the surgeon and the radiologist to determine whether this case is above or below the normal average.

We have done the same thing with the values in blood chemistry. So often, even the pathologist finds it difficult to remember normal values and range unless he is particularly interested in this field. It is great help to have before one's eyes at the bedside these accepted figures.

Dr. Kornblum has well demonstrated that there is much of clinical pathology that the radiologist should know. With such a knowledge, he can better cooperate with the pathologist, and by their combined efforts more accurate diagnosis will follow.

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# THE PRINCIPLES GOVERNING THE RADIATION THERAPY OF CANCER*

## AN ELEMENTARY LECTURE

*By* GEORGE T. PACK
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THIS treatise is not concerned with the indications and contraindications for radium and roentgen therapy nor with the relative merits of surgical and radiation treatment of cancer. It is assumed that the cancers selected for treatment by irradiation possess some degree of radiosusceptibility. Failure to consider this premise has led to the injudicious use of these physical agents with consequent loss of confidence in their effectiveness. The cancer must be more radiosensitive than the normal tissues which contain it, else radium and roentgen rays could offer no advantages over any destructive, non-selective cautery. The radiologist should decide, if possible, whether his therapeutic efforts are to be curative or palliative, insomuch as different biological and physical principles are involved. He also realizes that radiosensitivity and radiocurability are not synonymous; some highly radiosensitive tumors may become a generalized or systemic disease early in their course (lymphosarcoma), while other more radioresistant tumors metastasizing late (some neuro- and liposarcomas) are radiocurable by slow progressive radiation fibrosis.

The selection of tumors of radiosensitive behavior for treatment by irradiation requires a knowledge of the histologic and biologic factors determining radiosensitivity, a familiarity with the natural history of malignant tumors of all regions and considerable clinical experience in observing the response of these tumors to treatment. Tumors of embryonal origin are well known to be highly sensitive to radiation due possibly to their morphologic peculiarities and high metabolic rate. There are exceptions to this rule such as the adult testicular teratoma and some tumors of mixed cell origin. The number of mitoses and the degree of anaplasia are important factors in the determination of radiosensitivity yet only in a relative sense, as some cellular, undifferentiated, rapidly growing cancers (melanoma, neurosarcoma) are notoriously resistant to irradiation. Ewing has repeatedly emphasized the importance of the influence of the intrinsic properties of the cells of origin and Stewart has succinctly stated that "in the case of many individual tumors the fundamental nature of the tissue of origin outweighs all other considerations when an attempt is made to estimate the sensitivity." Thus, the primitive blood-forming tissues predetermine the radiosensitivity of tumors developing from their lymphoid, myeloid and vascular derivatives (lymphosarcoma, myeloma, endothelioma, angioma), and the various tissues arising from the neural crest cells almost uniformly give rise to radioresistant tumors (glioma, neurosarcoma, melanoma, mixed tumor of parotid). The nature of the tissue bed supporting the cancer is of fundamental concern, as every radiologist is cognizant of the difficulties and hazards encountered in irradiating cancer imbedded in cartilaginous, fat, osseous or fibrous tissue. Carcinomas are radioresistant in direct proportion to the extent of desmoplasia they excite. A soft, vascular stroma with tendency to cause a papillary structure of the tumor is more conducive to ischemic necrosis and rapid disintegration of the tumor under irradiation.

*Methods of Radiation Therapy.* There are

* Delivered before the New York Academy of Medicine, February 7, 1935.

two methods by which radiation may be applied to malignant tumors within the body. One uses an external source, either a roentgen tube or a radium applicator containing a large amount of radium. The rays must then traverse overlying normal tissues before reaching the tumor itself. The second method utilizes a source (radium) which is applied directly into the substance of the tumor or surrounding it. This source may be single or multiple. By this latter method the tumor receives 100 per cent of the dose and the surrounding normal structures much less. These methods may be designated as follows:

*External Irradiation.* A. Roentgen rays. (1) Low voltage source for superficial tumors. (2) High voltage and supervoltage sources for deep therapy.

B. Radium. (1) Teleradium therapy. Large quantity of radium (grams) in bomb or pack applied at considerable distance (6 to 15 cm.) for deeply situated tumors. (2) Superficial therapy. Small plaques, trays and moulages of radium for superficial cancers (lip, skin, etc.).

*Intracavitary Irradiation*—always radium. One or more filtered containers often in tandem arrangement and placed within the body cavities for contact application of radium against cancers in these locations, such as naris, orbit, antrum, larynx, esophagus, uterus, vagina and occasionally the rectum.

*Interstitial Irradiation.* Intratumoral or peritumoral placement of radioactive foci in form of radium needles or radon seeds. This method is useful in the treatment of accessible cancers, chiefly as an adjunct to external irradiation.

*Units of Dosage.* It is best to administer to all the neoplastic territory the maximal quantity of radiant energy compatible with the maintenance of tissue integrity. To speak intelligently of these quantities it is best to have some common physical and biological measures of the dosage. Thus in the case of radium the quantity of gamma rays at the source is known as the "dose of emission." One knows with precision the dose of emission because this is invariable. The dose emitted is expressed by two different notations. The one has for its basis the intensity of the gamma rays and the duration of their application; the intensity is proportional to the quantity of radium present; the dose is obtained by the product of the quantity and the time, which is expressed as milligram-hours of radium or as millicurie-hours of radon (gram-hours or curie-hours in the case of large radium bombs or packs). The other notation, which is utilized throughout France, makes the dose proportional to the quantity of radium emanation destroyed (disintegrated) during the course of its application (Debierne and Regaud, 1914). This is expressed in terms of "millicuries-destroyed" or of "microcuries-destroyed," the latter term connoting only one thousandth of the former. The physical efficiency of 1 millicurie of radon throughout its life is equivalent to 133 millicurie-hours. Therefore 1 millicurie-destroyed is equivalent to 133 millicurie-hours or 133 milligram-hours.

The dose of gamma or roentgen rays at the surface or the point of entrance into the body is the superficial dose while the dose to the tumor by unit volume of the tissues treated is the "tissue or tumor dose."

The unit of x-ray dosage called the "roentgen" or r (designated always by small r) has been standardized and internationally accepted. The roentgen has been defined as that quantity of roentgen radiation which, when the wall effect of the ionization chamber is avoided and the secondary electrons are fully utilized, produces in one cubic centimeter of atmospheric air at 0° C. and 76 cm. mercury pressure such a degree of conductivity by ionization that one electrostatic unit of charge is measured at saturation current.

In the measurement of roentgen rays and gamma rays by biological means, the most common unit is the establishment of

an erythema dose under certain conditions. Quimby of the Physics Department of the Memorial Hospital has defined and employed the term "threshold erythema," which is that dose of radiation that will cause a perceptible change in the skin of 80 per cent of the subjects and no discernible discoloration in 20 per cent in two to four weeks after the exposure to the rays. Quimby has found that the threshold erythema with 200 kv., 100 sq. cm. field, 50 cm. target-skin distance and filter of 0.5 mm. of copper and 2.5 mm. of aluminum is 500 to 525 roentgens. The therapeutic erythema, on the other hand, varies with different radiologists from 600 to 1000 roentgens.

*The Tissue Dose—Cancericidal Dose.* The tissue dose of a given volume of tumor is estimated according to the point within that receives the smallest quantity of energy. At the Memorial Hospital, all tissue doses are expressed in threshold erythemas. Although the quantitative basis is the best we have for tissue dosage, the response of various cancers to this same dose is qualitative and there is no absolute biologic unit to express this response. The determination of tissue doses at all depths below the skin surface and in tumors of all sizes and shapes is relatively simple with roentgen rays and external applicators of radium. The applicator dose necessary to produce the threshold erythema can be determined in each case by direct experimentation. The percentage of the amount falling on the skin which reaches various depths can readily be determined by means of water phantom and small ionization chamber. The tissue dose delivered in any mass by external irradiation may be considered as of that point which lies deepest or at the greatest distance from the skin portal. Every radiologist has isodose curves available for each type of external irradiation applicator and with this aid the determination of the depth dose for each tumor is greatly facilitated.

The problem is more complicated in interstitial irradiation. The most common interstitial sources used at the Memorial Hospital are gold seeds about 4 mm. long, 0.3 mm. in wall thickness and containing from 1 to 3 millicuries of radon. Experimental work by Quimby makes possible the determination of the percentage of a threshold erythema dose delivered at any distance from any gold radon seed imbedded in a tumor. It is necessary for every point within the region of the tumor to receive a certain minimum dose; and it is the tissue dose for the point receiving the minimum that should be calculated. It is most convenient to consider the sphere of tissue that will just contain the tumor to be irradiated. Martin and Quimby have shown that if a definite quantity of radon is to be used in any given sphere, it makes practically no difference in the dose on the periphery whether the radon be concentrated at the center or distributed uniformly within the inner half of the sphere. For purposes of approximation of dosage, they considered the radon to be concentrated at the center of the sphere that just contains the mass and calculated for the minimum the dose at a point on the periphery. Thus they were able to make a table giving the threshold erythema units for different quantities of radon in spheres of different sizes, which is of great value in the rapid calculation of dosage.

The practical value of these physical measurements is that the dosage of radiation is now on a rational rather than an empirical basis. The cancericidal doses for malignant tumors of the oral cavity, skin, breast, uterus, bladder, prostate, rectum and stomach have been determined and it is now possible to prescribe such a dose and the way it should be given, whether by external or interstitial irradiation or a combination of both methods. For example, intraoral squamous carcinomas require tissue doses of 6 to 8 T.E.D. while transitional cell carcinomas (Ewing) and lymphoepitheliomas (Schmincke) require 2 to 4 S.E.D for sterilization. To destroy the most

radioresistant mammary cancer may require a tissue dose of 10 threshold erythema units, although many radiosensitive carcinomas of the breast completely disappear after relatively small doses of external irradiation alone, when administered properly in fractionated doses.

*Prescription for Roentgen Therapy.* A correct prescription for roentgen-ray dosage is essential not only for purposes of record but also for the accuracy and safety of such treatments. A model prescription should mention the quantitative factor expressed in roentgens and the qualitative factor which is really the effective wave length of the beam of radiation. This may be expressed in Ångström units or by stating the half-value absorption layer of certain metallic filters. Most roentgen-ray records are not so explicit and the effective wave length of the beam is indicated by the kilovoltage and filter employed. The target-skin distance should always be recorded and if possible the target-tumor distance or tumor depth. The size of the field, i.e., skin portal, influences greatly the proportion of scattered radiation, so the dimensions must be given for each area treated. Finally, the time of application of the roentgen rays, whether the dose is given in a single treatment or fractionated over several days, completes the details of the prescription.

*Kilovoltage* (*Potential*). A high voltage current applied to a roentgen tube accelerates from the filament electrons of great velocity which by their impact on the target of the tube produces the radiation known as x or roentgen rays. As the voltage is increased the average wave length of the beam of radiation becomes shorter and shorter. The shorter the wave length of the radiation, the greater is the penetrating power of the beam. It is for this reason that the higher voltages (200 to 1,000 kv.) are employed in deep roentgen therapy, while superficial tumors as of the skin are usually treated satisfactorily by low voltage roentgen rays. As the voltage is increased it has been found advisable to increase the filter accordingly in order to exclude the long, more easily absorbed and harmful rays. No roentgen beam as emitted by the target is truly homogeneous and the radiation produced in supervoltage tubes has its quota of long, feebly penetrating rays which must be filtered out if the full effectiveness of the short-wave components of the beam is to be obtained. It has been estimated that one and a half million volts produces roentgen rays that approach in quality or shortness of wave length, the gamma rays of radium.

*Electrostatic Production of High Voltage Roentgen Rays.* The development of electric generators during the last one hundred years found its most suitable embodiment in the application of Faraday's principles of electromagnetism. Modern high voltage technique has evolved almost entirely under this influence until the present time. One of the first of the several "million volt" roentgen machines used for cancer therapy in the United States was the cascade tube designed by Coolidge, Dempster and Tanis, for operation at a maximum of 900 kv. and which was kindly loaned to the Memorial Hospital by the General Electric Company in 1931. This high voltage generator is a special induction coil to which is applied 60 cycle alternating current at a maximum of 1,100 volts. Although these electromagnetic generators have been improved and the limits of their applicability in the treatment of cancer by high voltage roentgen rays have not been attained yet there are some valid reasons for reconsidering the possibilities of electrostatic generators. Van de Graaff was aware of the great expense, complications and inherent defects of an impulsive, alternating or rippling source of current, the necessary large size of the electromagnetic generators and the fact that the efficiency of high voltage alternating current devices decreases rapidly as higher voltages are sought. Van de Graaff therefore devised an electrostatic generator of current based on the sugges-

tion of Kelvin that the charges should be carried to the electrode on a belt conveyor consisting of alternately insulated metal segments. His electrostatic generator required a conducting terminal, its insulating support and a means for conveying electricity to the terminal, which needs were met by a hollow metal sphere supported on an insulator and charged by a rotating belt conveying electricity from earth potential and depositing it within the interior of the sphere. He has constructed four models, three being successive developments of generators operating in air and designed respectively for 80,000, 1,500,000 and 10,000,000 volts, and the fourth being an essentially similar generator operating in a highly evacuated tank. It is this last type, which, when equipped with a suitable target, may eventually be one of our main sources of therapeutic roentgen rays. The upper limit to the attainable voltage is said by Van de Graaff to be set by the break-down strength of the insulating medium surrounding the sphere and its size, while the upper limit to the current is set by the rate at which the belt area enters the interior of the sphere, carrying a surface density of charge, whose upper limit is that which causes a break-down field in the surrounding medium. Van de Graaff added a refinement to this apparatus by the addition of an induction device whereby charge of the opposite sign was carried by the belt on its return journey, thus doubling the current output. A second refinement consisted of a self-exciting charging device by means of which an external source of electricity was not heeded. Although this outfit has not been used to treat cancer as yet, its perfection may well be one of the signal advances in radiation therapy.

*Comparison of Teleradium Therapy with Supervoltage Roentgen Therapy.* The interviews recently given to the lay press concerning the ultimate substitution of supervoltage roentgen rays for radium and the consequent great economic loss to cancer institutes possessing large quantities of this valuable element are misleading and incorrect. Radium in the form of an external applicator such as a "bomb" or "pack" will probably be supplanted by roentgen therapy, but the great value of radium remains, as it always has been, as the means of interstitial and intracavitary irradiation. External irradiation, however proficient and applicable it may become, will scarcely displace radium, especially in its employment in emanation plants.

A comparison of teleradium therapy with an element or emanation pack and roentgen rays of a million volts will show little difference in biological effects with similar standards for control, if the same factors such as time of application and tissue dose delivered are considered. The million volt roentgen rays, because of the greater intensity of radiation, can treat many more patients in a given time, but this intensity may not be desirable since we now know that prolonged or continuous irradiation has many advantages. This roentgen-ray outfit entails greater expense for maintenance and repairs and in some respects is less adaptable and flexible than a radium pack. The usual radium pack contains 4 grams of radium. If Van de Graaff's ten million volt electrostatic machine could be mounted in a vacuum and equipped with a tube, it would produce a beam of roentgen rays as intense as that which would emanate from an applicator containing 5,000 tons of radium. Roentgen rays produced at voltages greater than 1,500,000 are of a wave length comparable to the gamma rays of radium.

*The Effective Wave Length of Radiation.* The wave length of roentgen rays depends on two factors: the energy given to the electron and the atomic weight of the target. The greater the atomic weight of the target, the shorter will be the wave length of the characteristic radiation. The targets of most roentgen tubes used in therapy are composed of tungsten, therefore this is a fixed factor. When the roentgen rays enter

the body the targets encountered are of low atomic weight (sodium, potassium, calcium, etc.), therefore the secondary waves or photons are of long wave length and feeble penetration. The higher the potential applied to a roentgen tube, the greater will be the energy of the impinging electron, the shorter will be the effective wave length and the greater will be the penetrating power of the beam. Therefore by increasing the potential or kilovoltage, increasingly shorter wave lengths are produced, the advantage of which lies mostly in their deeper penetration and the delivery of greater depth doses to tissues. Herein is the gain achieved by the advent of supervoltage roentgen rays. Failla has found that the relative depth doses at 10 cm. depth obtained under comparable conditions with 200 kv. roentgen rays, 700 kv. roentgen rays, and gamma rays, are respectively 29.0, 41.2, and 56.7 per cent. Accordingly from this point of view, 700 kv. roentgen rays are considerably better than 200 kv. roentgen rays, but not so good as gamma rays. This advantage is not realized in clinical practice because it is not practical to apply radium at the focal distances used in roentgen therapy.

Although we have said that the relative values in radiation therapy of the different wave lengths depend on their penetrating power rather than on essential differences in biological effectiveness, we do not mean that there is no differential effect on tissues. F. C. Wood states that the only difference in the electrons from very high voltage roentgen rays and low voltage roentgen rays is the difference in speed of the electron and he states that this cannot produce much difference in effect. We cannot subscribe wholly to this dogma. In the first place, the number of ions produced per unit length of path of particles travelling at high speed depends on the speed of the particles. There is experimental evidence to prove that the greatest concentration of ions occurs near the end of the path, when the speed of the particle is relatively low. This difference in concentration of ions depending on the speed of the electron must alter the rate of recombination of ions, which causes the chemical changes on which, presumably, radiation effects finally depend. Furthermore, we have clinical and experimental evidence to show that there is a differential action of radiation of different wave lengths in the case of normal (skin) and pathological tissues in the human body.

*Ionization in Tissues.* The lethal action of radiation on the cell is due to the absorbed energy, which results from the impact of the gamma or roentgen rays upon the atom and the release of electrons inside of the cell. The sequence of events in the cell seems to be triple: (*a*) ionization, (*b*) chemical changes, and (*c*) biological effects. This subject having been considered in detail by Failla in his paper on "Ionization and its bearing on the biological effects of radiation," it will be merely mentioned here. The initiation of the processes leading to the death of the cell is started by the transfer of energy from the beam of radiation to the matter of the cell. The phenomenon of ionization results when radiation (the particle of which is called a photon) transmits energy to an atom in its path with a resultant release of an electron traveling at high velocity and in turn expending this energy by removing still other electrons from atoms in its path. The two processes by which this transfer of energy from photons to matter takes place are (Failla[3]):

(A) The photoelectric effect in which case all the energy of the photon is transformed at once and the secondary electron leaves the atom with a kinetic energy less than that of the photon by the amount necessary just to separate the electron from the atom, (B) the Compton effect, in which case the transfer of energy from the photon to the electron takes place according to the laws of elastic impact, and depends on the angle which the path of the emergent electron makes with the path of the impinging photon. A photon can transmit

practically all of its energy to an electron in the event of a head-on collision which sends the electron hurtling through space substantially in the direction which the photon would have followed had it not been stopped. If the electron is projected in any other direction the energy imparted to it is always less than this amount; its speed is lower and the number of ions which it can produce is smaller.

No electrons can be emitted backwards towards the source of radiation and at most they can be projected only at right angles to the path of the photon. But they necessarily deviate somewhat from their initial course because of impacts with atoms in their path and so eventually after deflections and pursuance of a zig-zag trail may travel in the opposite direction. The remaining energy of the impinging photon after an electron has been set free from the atom by the Compton effect is spent as a new photon of less energy, longer wave length and less penetrating power. These photons also undergo the same transformations and on impact with atoms release their energy to electrons or beta particles which contribute to further ionization in the tissues. With an increase in the intensity of radiation, there is a corresponding augmentation in the quantitative production of ions in a given time due to the greater number of beta particle tracks, called by Failla "ionization loci." As stated previously the concentration of the ions along the tortuous path of these high speed electrons varies according to their velocity and is greatest near the end of the electrons' course where the speed of the particle is relatively low.

When an atom on impact loses an electron (a negative charge), the atom then has a positive polarity and may reunite with the freed electron or any other electron in its neighborhood. The wandering electron may attach itself to an atom forming a negative ion. An interchange of electrons takes place when these ions of different polarity come together, so that neutral atoms with resultant chemical changes follow these recombinations. This process of recombination always accompanies ionization; both occur constantly in tissues which are being irradiated. Not all such effects of ionization and recombination are responsible for biological changes because the chemical transformation may be harmless to the cell. Nevertheless it seems entirely reasonable to assume that the ultimate way in which radiation affects living tissues is by those chemical changes induced by ionization and recombination.

*Current* (*Milliamperage*). The current in milliamperes and the time required to deliver a given amount of energy are inversely proportional to each other. The milliamperage is essentially a measure of the number of electrons which strike the target. The usual roentgen tubes carry from 4 to 30 milliamperes. Thus a tube running at 4 milliamperes for twenty-five minutes would deliver 100 milliampere-minutes and a tube running at 25 milliamperes for four minutes would also deliver 100 milliampere-minutes or its equivalent in roentgens, other conditions remaining the same.

*Filter.* The penetrating power of the radiation or the quality of the beam may be changed by the interposition of filters (usually metallic) between the tissues to be treated and the source of radiation. Soft radiation of long wave length limits the effectiveness of the beam and lessens the relative amount of the beam which reaches the deeper tissues containing the tumor. The filter will remove these soft destructive waves and permit the shorter wave lengths to pass through and enter the deeper tissues and tumor, thus affording a greater depth dosage with less skin and surface reaction. A statement of the effective wave length is one of the ways of expressing the penetrating power, or hardness or quality of the roentgen-ray beam or the beam from a source of radium. The effective wave length is expressed in Ångström units. The quality of the radiation beam may also be stated as the "half-value layer" which is

the thickness in millimeters of the filter (e.g., copper) sufficient to reduce the intensity by half. Failla and Quimby have found that the effective wave length employed in the usual deep roentgen therapy at the Memorial Hospital is about 0.16 Å. This treatment is given with 200,000 volts (peak), filtered by 0.5 mm. Cu and 1 mm. Al. With intermediate voltage of 140 kv. the filter may vary from nothing up to 6 mm. of aluminum; with a filter of 4 mm. Al the effective wave length is about 0.25 Å.

In the case of radium, the filters employed, usually brass, lead, silver, gold or platinum, are usually expressed in the equivalents of certain thicknesses of platinum. One millimeter of platinum or its equivalent (occasionally 0.5 mm. platinum) is the customary filter for surface applications of radium or teleradium therapy. Intracavitary radium treatments are given with filters of 0.5 to 1 mm. of platinum, while interstitial irradiation requires considerable less filtration. Gold radon seeds have a wall thickness of 0.3 mm. gold and most platinum needles for interstitial use are designed with a wall thickness equivalent to 0.5 mm.

*Size of the Field of Irradiation.* Failla and Quimby have derived a formula by which the amount of radiation effective at any tissue depth for all practical conditions of treatment may be obtained. This formula takes into consideration, as must all quantitative estimations of dosage, the area of irradiation or the size of the skin portal. In brief, we may say that the larger the field, the greater will be the secondary and scattered radiation which is produced in the body of the patient. These rays may amount to as much as 40 per cent or more of the total irradiation. At a depth of 10 cm., with a large field, probably 80 per cent of the radiation is of this type. The area treated therefore receives the sum of the primary beam plus the part of the secondary rays which traverse it. These facts are taken advantage of in therapeutics; to give as great a depth dose as possible from one or more portals (e.g., in the oral cavity) the beam is directed with great accuracy through as small a portal or field as possible, since by this means the superficial dose at the portal of entry may be much higher with less skin damage than when a larger portal is employed.

*Target-Skin or Radium-Skin Distance.* The inverse square law of radiation states that the intensity of a beam of roentgen rays or gamma rays varies inversely proportional as the square of the focal-skin distance from a point source. Thus the radiation intensity from a high voltage roentgen tube at 50 cm. distance is almost twice that delivered at 70 cm. focal-skin distance. Or a radium applicator placed at 2 cm. radium-skin distance conceivably would deliver four times the superficial dose as the same applicator applied for the same time at twice the distance or 4 cm. (This is not exactly true since the radium applicator is not a point source.) This fact may be expressed also in the following manner. Since the dose is dependent on the product of the intensity times the duration of exposure, the radium treatment at 4 cm. distance would require four times as many minutes or hours as at 2 cm. radium-skin distance. The question naturally arises —why not decrease the focal-skin distance as much as possible to save time and expense? In the case of very superficial non-infiltrating skin cancers this plan is feasible but for more deeply situated cancers the depth or tissue dose is increased (in comparison to the dose delivered to the superjacent skin and tissues) with the greater skin-target distance. Theoretically the distance might be increased sufficiently so that the relative dose on the skin at the portal of entry of the rays would be almost the same as at the location of the tumor within the body.

*Heublein Method of Continuous Irradiation.* The late Dr. Arthur C. Heublein gave the Memorial Hospital a radiation unit designed to give continuous irradiation of low intensity and short wave length to the

entire body. Intermittent teleroentgen therapy had been tried previously in England and Germany with inconclusive results. This clinical experiment was carried out by Heublein and Craver in 134 cases over a period of two years. Craver concluded that it was a valuable addition to the treatment of several generalized and radiosensitive tumor processes, such as the leukemias, lymphosarcoma, Hodgkin's disease and multiple myeloma, and that its results in the treatment of chronic lymphatic leukemias and pseudoleukemia seemed superior to any obtained heretofore by local irradiation. The treatment unit consists of a four bed ward with a Coolidge tube, operating at 185 kv. and 3 ma., placed near the ceiling behind the most distant wall. The patients placed at 18 feet and 24 feet from this source of radiation were continuously exposed to the beam of roentgen rays at this great distance. By an electric timing device it was determined that the patients averaged about twenty hours of exposure daily, the time out being due to nursing care and other interruptions. Considering 750 r measured in air as the clinical skin erythema dose for a single high voltage roentgen treatment, the time required to deliver a 30 per cent dose or 225 r to a patient in the bed at 24 feet target-skin distance was 250 hours, so at the rate of twenty hours of exposure daily, this dose could only be administered in 12.5 days. In the treatment of leukemia, Craver was particularly cautious but in other diseases he eventually increased the doses to 50 or 60 per cent S.E.D. (375 and 450 r) with no complications except the occasional development of leukopenia, anemia and thrombocytopenia in some cases. This work is one of the most important achievements in radiation therapy during the last decade and its principles of low intensity, great distance, continuous irradiation and long duration of treatment may soon be applicable in the local treatment of cancers that have otherwise remained refractory to present methods of applying radiation.

The possible advantages[1] originally listed by Heublein were:

(1) The nearly uniform distribution of the rays throughout the body in treating generalized neoplasms; (2) the possibility that great protraction of treatment would make possible the irradiation of all the tumor cells during their period of mitosis when they are most sensitive and (3) the assumption that despite the protraction of treatment the intensity of radiation affecting any given cell would nevertheless remain sufficient to sterilize it.

*The Time-Intensity Factor.* It seems logical to assume that a cancer cell or a tissue cell would not be indifferent to variations in the intensity of radiation. Such a cell continuously engaged in self-repair, the ingestion, consumption and storage of food, the excretion of waste products, the pursuit of its specific function and possible preparation for cell division is a living unit and must be capable of making certain adjustments to the influences of noxious agents to which it is exposed, whether they be chemical or physical. All physiological processes require time for their completion. If the doses were equal, the cell—either normal tissue cell or cancer cell—should be more tolerant of prolonged irradiation of low intensity than of short irradiation of high intensity. The end-result of successful external irradiation is the destruction of the cancer cell and the preservation of the normal tissue cells; there is experimental and clinical evidence to indicate that long duration and low intensity of irradiation (within limits) has greater differential effects on tumor cells than on normal tissue cells. As will be shown later, the explanation of this fact is that the normal tissues possess greater recuperative power which is taken advantage of in the increased duration of irradiation. The low intensity and longer time of irradiation permits the accumulation of a much greater total dose than could possibly be given in a single massive treatment. The tumor cannot be removed from the body for treatment by irradiation, therefore the maximum dose

which can be delivered to it from external sources of radiation is limited entirely by the tolerance of the tissue which contains it.

The answer to the question whether or not the normal and cancerous tissues might vary considerably in their differential reactions to changes in the time of irradiation by roentgen rays or radium has been provided by Regaud and his collaborators —Coutard and Lacassagne. They compared the effects produced on the anorectal skin and mucosa and the testicular tissues of the rabbit and ram by selected doses of radiation delivered in different times. The testicles of mammals were chosen for these experiments because their behavior and structure closely resemble that of malignant tissues, e.g., frequent cycles of cellular reproduction, active mitosis and radiosensitivity. This analogy between mammalian testicles (in a state of active spermatogenesis) and malignant tumors is also apparent in their response to roentgen and gamma rays. Regaud found that it was impossible to sterilize the testicles of the rabbit by the administration of a single massive dose of roentgen rays without causing serious lesions of the skin. If, without altering any of the other experimental conditions, he modified the chronological distribution of the dose, dividing it and lengthening the time of its administration, he observed a remarkable difference between the effects produced on the anorectal integuments and on those produced on the testicle. The effect on the integuments was attenuated and lessened while the effect on the testicle was increased. These studies on spermatogenesis and similar clinical experiments on the roentgen and radium treatment of epidermoid carcinomas furnished Regaud and Coutard with the data from which they formulated their theory of radiation therapy. Regaud's explanation of the superiority of continuous or fractionated irradiation over short intensive treatments is founded on the existence of alternating periods of radiosensitivity and of radioresistance in the life of the spermatogonia (in the experiments) and the cancer cell (in clinical practice). Spermatogenesis in a mammal such as the rabbit is a continuous phenomenon if the testicle is considered as a whole. But if one considers only a certain cell or line of cells on a seminiferous tubule, the function of reproduction by cell division is seen to be discontinuous and cyclic and the spermatogonia-like cancer cells, pass through alternating phases of multiplication (brief phases) and of rest (long phases). In one line of cells, either spermatogonia or cancer cells, the phase of multiplication corresponds to accentuation of radiosensitivity (law of Bergonié and Tribondeau), whereas the phase of rest corresponds to a diminution in radiosensitivity. A short treatment therefore might destroy only those spermatogonia or cancer cells which are dividing at that time; it spares the others. It is only natural that prolonged and continuous irradiation (in the case of radium) or well fractionated irradiation with proper spacing of the fractions into a fairly long time (in the case of roentgen rays) is more efficient than brief intensive irradiation, because in the first case the germinal or cancer cells are killed one after the other as the cycle progresses and these cells enter for the moment the phase of maximal radiosensitivity.

These principles are now so generally recognized that the prolonged irradiation of low intensity or fractionated cumulative treatments have found almost universal favor with roentgenologists and radium therapists. These treatments depend usually on the administration of suberythema doses repeated every twenty-four to forty-eight hours until a total dose of 6 to 8 threshold erythema units may be delivered to one skin portal with perfect safety. To illustrate the application of this principle, let us consider the treatment of a hypopharyngeal carcinoma by high voltage roentgen rays only. Two lateral portals are used to crossfire the beams of radiation.

With a single massive dose, only 850 r can be given to each side of the neck without seriously damaging the skin. By the fractionated method 300 r may be given daily alternating on each side of the neck until a total of 3,000 to 4,000 r are delivered through each portal. Such a course of treatment requires three weeks to consummate the dose required to sterilize the carcinoma.

*Recuperation of Normal and Neoplastic Tissues.* The advantages of prolonged irradiation of low intensity or fractionated cumulative treatments are probably explained by the differential recuperation of normal and neoplastic tissues. This fact can be appreciated best by reviewing the accepted four common methods of treatment: (*a*) the massive dose technique, (*b*) saturation dose, (*c*) fractionated dose and (*d*) continuous irradiation. By the massive dose method the full tolerance of the skin and normal tissues is exhausted by a single maximal exposure to radiation, so that this dose cannot be repeated for a long time. The tumor within the tissues, while profoundly affected, possibly even to a greater degree than the skin, still may survive this single dose and ultimately recover. Presumably normal tissues have much greater powers of recuperation than do neoplastic tissues, i.e., their rate of recuperation is faster. This fact can only be inferred from abundant clinical evidence at hand and from the comparative studies of Henshaw on adult and embryonal tissues. Duffy has shown that human skin can recover 69 per cent of the immediate damage in twenty-four hours and 76 per cent in forty-eight hours following the administration of a threshold erythema dose (525 r). The saturation principle was first described by Kingery who applied it in the treatment of skin diseases by unfiltered low voltage roentgen rays. Briefly, it consists in the initial administration of an erythema dose and then maintaining the biological effect so produced by the addition of smaller doses at proper intervals. Kingery estimated that he could add 50 per cent of an erythema dose at the expiration of three and one-half days, to substitute for the 50 per cent depreciation of the original dose. Pfahler first successfully applied this principle to the treatment of cancer by properly filtered high voltage roentgen rays. In the fractionated method, previously described, a daily suberythema dose is given until a maximal effect is obtained. The dose given every twenty-four to forty-eight hours is greater than the recuperation during the same period so that finally a cumulative effect is obtained. Our clinical experience leads us to believe that the results from this method are superior to the other two, possibly because the time interval and low daily dosage permits sufficient recuperation of normal tissues to maintain vitality in the irradiated part, while the more slowly recuperating cancer receives a total dose that is cancericidal. This principle has been applied by Craver still more in continuous irradiation by the Heublein teleroentgen method. We may sometime find that we shall be treating cancer by the installation of numerous small roentgen units each operating at low intensity and irradiating patients through heavy filters and at relatively long distances for eight to twelve hours daily over a period of weeks. Then we should be taking full advantage of the difference in the recuperative abilities of normal and cancerous tissues.

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# A CRITICAL STUDY OF THE USE OF THE LEAD PERFORATOR AND RECIPROCAL IN RADIATION THERAPY*

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IN THE radiation treatment of deep-seated malignancies, we often feel that our failures are due to insufficient radiation. Those abroad who have had better results have been using very large doses, and have ignored the harmful effect of such radiation on the overlying skin. Here (in America) we are more thoughtful of the skin, and we are timid in the use of large doses of radiation on account of the harmful effects on the skin. I am presenting a method of protecting the skin against permanent injury when large doses of heavily filtered radiation are used. The theoretical basis for this method was originally described by Köhler[2,3,4] and by myself[5] independently. The principle on which the method is based is well known to all radiotherapists, that small skin areas will tolerate much heavier doses of roentgen rays than larger areas. Apparently the close proximity of the normal skin protects the small irradiated areas from necroses. Furthermore, if necrosis does start, rapid replacement by the closely adjoining epithelium is fostered.

The device here employed (Fig. 1), to convert large skin areas into numerous small ones, is a lead sheet about 2 mm. in thickness, 20 cm. square, with many uniform, regularly spaced perforations, comprising a definite percentage of the total square area. When placed over the skin of the portal of radiation the screen divides the single portal into three to four hundred small islands, through which the radiation is delivered, leaving a network of normal skin protected from the radiation.

The exact size and shape of the perforations can, of course, be legion. In fact, numerous patterns (squares, lozenges, checkerboard effect, ovals, hexagons, and circles, comprising one-half, one-third, one-quarter, of the total square area) were tried for the first four months, before the choice was made of the perforator which has 0.5 sq. cm. circular perforations, to each square centimeter of space (Fig. 1).

Since the radiation is of streamer type, we had to investigate some of its physical and biological differences before we could apply it clinically. The summary of our findings of the physical investigations from the practical viewpoint are:

(1) That the quantity of radiation at any depth bears the same relation as the area of perforation bears to the entire area of the lead screen under irradiation. In other words, if the perforated area is one-half of the square area of the screen, the quantity of radiation will be one-half of what *it would be* if no perforator were used. At depths over 5 cm. the quantity of the radiation is slightly more (up to 3.5 per cent) than the theoretical 50 per cent.

(2) That the back-scattering reaching the skin covered by the perforator isthmuses is from 20 to 25 per cent of the total radiation, and therefore sets the limit of safe radiation at four erythema doses, if we expect the protected skin to act as centers for re-dermatizing the treated areas.

(3) That the radiation emerging under the perforator being of the streamer type, it is not homogeneous unless a large focus tube is used. But this is not of biological significance, as will be shown later. It can easily be obviated by shifting of the tube and delivering one-quarter of radiation

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from each of four different points. The shift is according to arithmetical proportion.

*Biological.* The physical work indicating the possibility of delivering increased doses of radiation through the perforator up to the limit of back-scattering. The intermediate step before applying the method to man was to learn if the streamer radiation is as effectual in limiting growth as ordinary radiation. For this study chicken ova, white mice, and rabbits were used. The results with the ova were strengthening the contention that the streamer radiation is as good as the ordinary radiation, if the doses are not less than one erythema. However, if the dose is less than erythema, the streamer radiation is not as effectual in delaying the development of the embryo. The studies on the mice were made by placing the animals in ventilated wooden cages, with paraffin phantoms above and below the animal, considering the animals as tumor masses, and one, two and three erythema doses were given to each group with and without the perforator. The comparison shows that the perforated radiation has at least as much destroying influence on the mice as the ordinary radiation. The majority of those treated with the perforator died sooner than those without the perforator, using the same quantity of radiation. In treating the rabbits, the clinical conditions were approximated as closely as possible. The buttocks and backs of the rabbits were shaved chemically, and the dose necessary to cause slight ulceration and crusting on the control side was first determined. Then three or four times this dose was delivered through the perforator to the other side. There was no crusting or ulceration seen within twenty-one days. This represents a definite gain of 100 per cent on the radia-

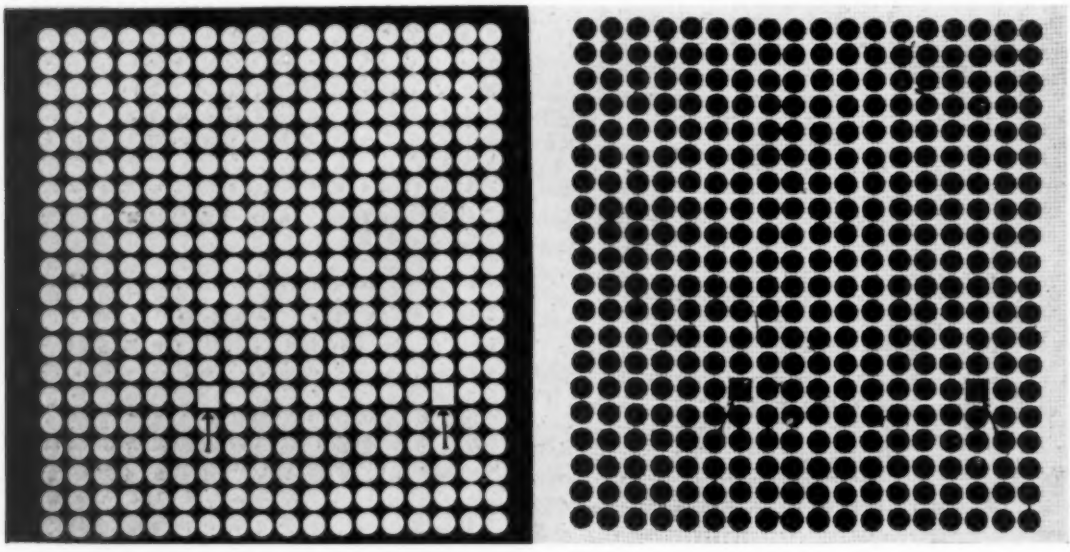

Fig. 1. On the left is a photograph of the lead perforator consisting of a sheet of lead, 20 cm. sq., with perforations of 0.5 sq. cm. to each square centimeter of lead. Note the two eccentric square perforations, also the wide margin of lead on the left. These are used for replacement of the perforator in the identical position on the skin when the entire dose is not given in one sitting. On the right is a photograph of the reciprocal perforator, made by placing the lead cutouts in a perforator and soldering each cutout disk, as well as the two squares, to a very fine wire copper gauze; then the edges of the gauze are dipped in a thick aceto cellulose solution. After it dries, the disks are pushed out of the perforator. This process gives an exactly mounted reciprocal of the perforator. The copper gauze is used as base for the purpose of holding the disks in proper position, and also to enable the use of the reciprocal on round or angular surfaces.

tion, and greater safety to the skin if the perforator is used.

*Clinical.* The most important part of this investigation, the clinical, suffers from lack of extensive material. It is in the hope that radiotherapists with extensive material at their command may study this method more fully and find it of use to them that from the radiation, the tumor mass is irradiated through a second, a third or a fourth portal, and after four weeks, the first portal is again ready for treatment through the area formerly left unexposed and protected by placing the *reciprocal perforator*, and treating through it, again giving twice the quantity of radiation. This

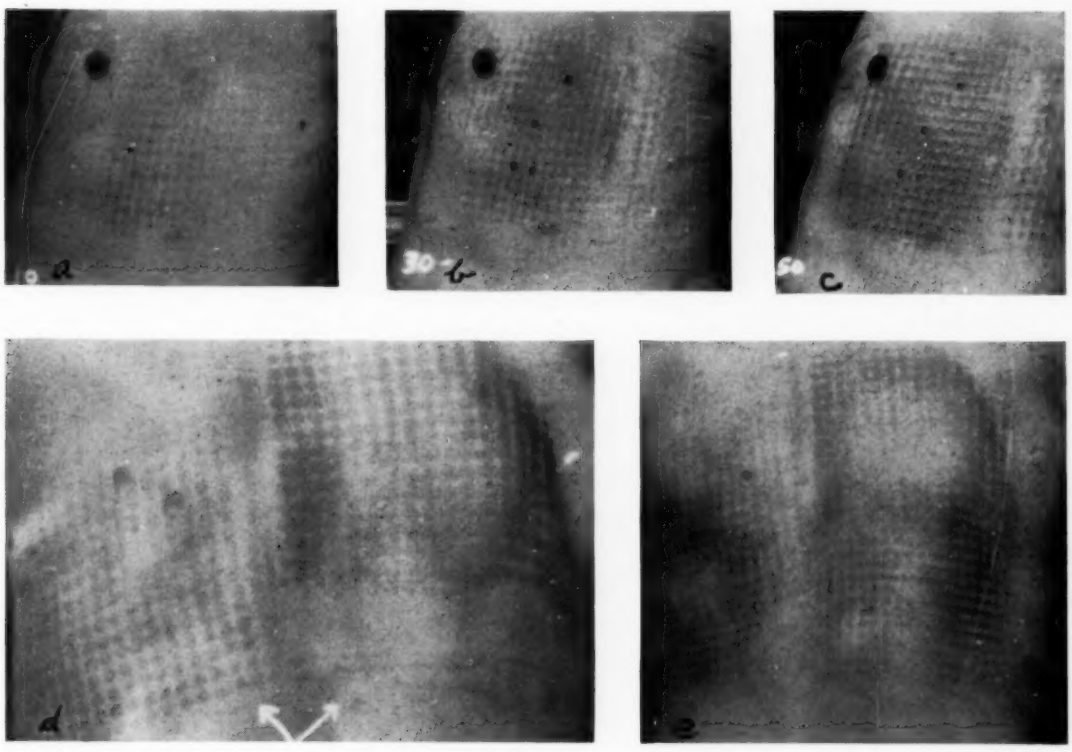

FIG. 2. This figure is taken from photographs of a patient's chest at different stages of the treatment through the perforator and the reciprocal. The dark spots are from the application of mercurochrome used as painted markings to facilitate replacement of the perforator or reciprocal over same area, when entire dose is not given in one session. *a*, the appearance of the skin ten days after initial treatment with perforator; *b*, thirty days after initial treatment with perforator, and two days after treatment with reciprocal; *c*, fifty days after initial treatment with perforator and completion of treatment with reciprocal; *d*, one area after completion of treatment through perforator only (area on left); another area about half way of treatment through reciprocal; *e*, same area as *d* after all treatment through perforator and reciprocal has been completed. Note that first area treated (upper right quadrant) is fading slightly; while lower left is just about at the maximum point of reaction.

this paper is presented. The advantages of the method are manifest—the main one being that the amount of radiation delivered to a deep-seated lesion can be increased to more than twice the usual amount of radiation, without permanent injury to the skin; and again, that while the skin, over a single portal, is recuperating makes a total of four erythema doses without injury to the skin.

The disadvantages are of minor importance when compared with the advantages. If the treatment is stopped in the middle, there is a mark of the perforator left on the skin for many months (Fig. 2), but this disadvantage can be obviated by re-irradi-

ating through the reciprocally patterned perforator (Fig. 1) four weeks after the original irradiation.

The treatment is more expensive in time and money, since it takes twice as long in actual radiation time to deliver the same number of roentgens through the perforator as without it. Finally, this method of treatment requires more precise planning and knowledge of therapy than the more stereotyped ones.

The method as proposed for the treatment of deep-seated lesions is as follows: The lesion, in as exact shape and size as possible, is mapped out on a topographical cross-section film of the body at the segmented level involved, and the smallest "streamer" which will cover the lesion by a narrow margin is mapped out (Fig. 3). These streamer lines represent the angle, the point of entrance, the spread and the point of exit of the rays as they appear after passing through the perforator. Care is taken that the streamers meet in the area of the tumor, and not at either the entrance or exit portals. The total dose is now computed from the dosage charts and to each portal a definite proportion of the total radiation is assigned. The perforator is fastened by adhesive to the first portal.

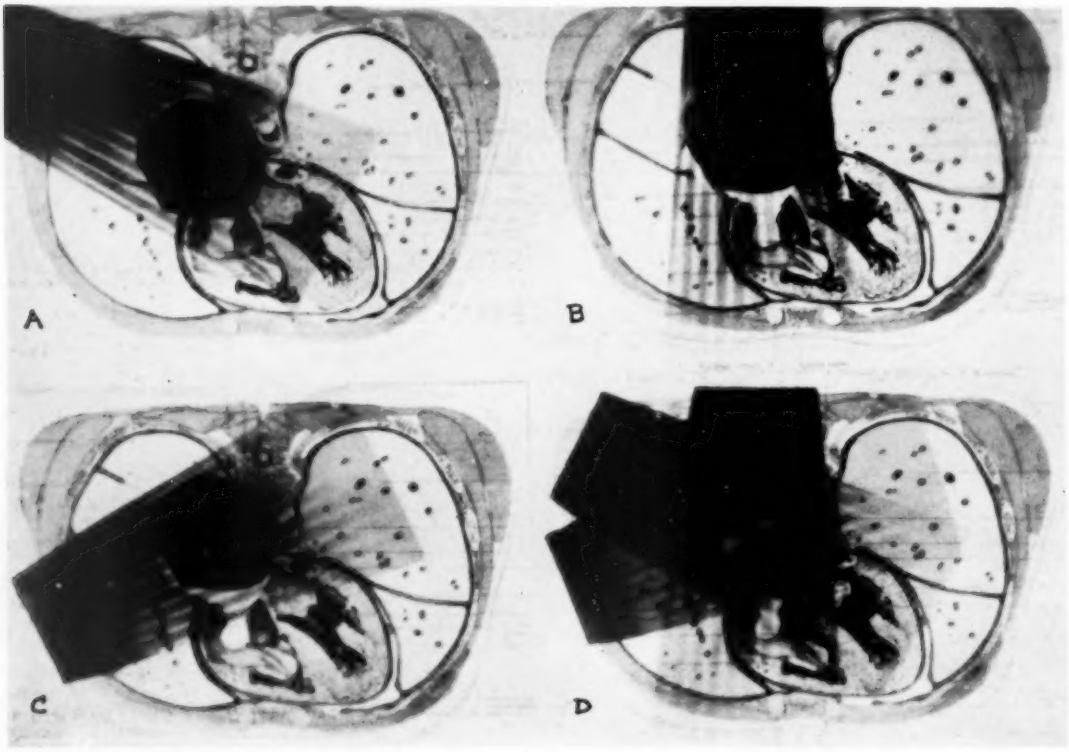


Fig. 3. This shows the plan of arrangement of the areas and direction of radiation in a tumor of the lung. In *A* the tumor is plotted on a topographical cross-section through the 7th thoracic vertebra (center of location of tumor). A streamer of a width large enough to cover the tumor by a small margin is placed over the cross-section. The streamer gives the approximate size of cone or opening to be used on the area to be treated. In *B* another suitable streamer is placed from a different field, but not overlapping either the entrance or exit of the radiation of former area. *C* shows the third streamer arranged similar to the first and second. These streamers give a rough estimate of the percentage of radiation. In *D* we note that according to this size of tumor we cannot use more than three fields, otherwise the entrance or exit of the radiation from one field would meet another, which makes the calculation of the dose even more difficult.

One-fourth of the radiation is now given from each of four points, if homogeneity is desired. If the focal spot of the tube is large, the total radiation can be given without shifting the tube.

Often the machine, the tube, or especially the patient is not able to tolerate the lengthy radiation of three to four erythema doses for a portal at one sitting, and the question arises if the dose may be delivered during several sittings. If the skin under the two eccentric square perforations (arrows in Fig. 1) is painted with mercurochrome, or some other non-roentgen-ray absorbing dye, the perforator may be replaced exactly over the same skin area the next day, so that the radiation may be divided over a several day period. Sometimes a paraffin cast must be made and set against flexible parts of the body, such as the neck, in order to assure the exact replacement of the perforator the next day. This fractional method of treatment has a further advantage in that the patient is being constantly irradiated (daily or every other day) for two months, the first month being devoted to the irradiation of the original three to four portals through the perforator, and the second to the irradiation of these same portals through the reciprocally patterned perforator. In this way the tumor is constantly irradiated and the skin has the maximum opportunity to recover from the treatment.

I would also like to state at this point that we have not yet exhausted all the different means of protecting the skin from the deleterious effects of large doses of roentgen rays. In our laboratory, we have used lately, in addition to the perforator and reciprocal, the cooling effect on the skin according to the tissue researches of Spear,[6] a flat ice cap being used during and for the first forty-eight hours after the treatment. So far, we feel that the reaction produced in the skin by six erythema doses when cooled for the first forty-eight hours is not greater than the reaction produced on the skin with four erythema doses not cooling the skin, both of course have been used with the perforator and reciprocal. To me it seems that this subject deserves a detailed report with description of the special single cooling system that can be used in a ward to cover one or more areas of a dozen patients under this form of therapy. The type of pancake cooling bag connected to the cooling system and its various forms and shapes to fit into different parts of the bodies used should be separately reported.

Up to the present, 50 cases, mainly inoperable tumors of the head, neck, lungs, esophagus and long bones have been treated by this method. Although no definite conclusions can be drawn because of the paucity of material, we still feel that in esophageal and lung tumors, our statistics may be improved by the use of this method, prolonging at least the average duration of life, if not effecting a cure.

The work on this method of irradiation has been presented in its unfinished state mainly to indicate its possibilities to other workers in the field of radiotherapy. Perhaps with their help a clinical study of the best type of perforator, of optimum size, shape and pattern, will be successfully conducted

## SUMMARY

A method of delivering unusually heavy doses of roentgen rays without permanent injury to the skin is proposed. If, instead of a large portal, numerous small ones are used, about twice as large a dose can be safely delivered to the underlying tissues. The skin portal is divided into numerous irradiated and protected areas by use of a lead screen with multiple perforations. The network of skin areas protected from radiation by the lead apparently keep the small irradiated areas from necrosing, and act as centers of healing if necrosis does begin. This surgical principle permits increased dosage without permanent injury to the skin, and fits the method for the treatment of selected cases of malignancy. The pro-

tection of the skin by this method is increased 40 to 50 per cent by cooling of the irradiated area during the first forty-eight hours after the treatment.

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*Assistant Editor:* Ruth Bigelow, 110 Professional Building, Detroit, Mich.

*Editorial Board:* A. C. Christie, E. H. Skinner, Lauriston S. Taylor.

*Advisory Board for Pathology:* James Ewing, Eugene L. Opie.

*Thirty-seventh Annual Meeting:* Cleveland Hotel, Cleveland, Ohio, Sept. 29-Oct. 2, 1936.

### THE AMERICAN RADIUM SOCIETY

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*Janeway Lecture Committee:* Curtis F. Burnam, Chairman, Baltimore, Md.

*Committee on Arrangements:* B. P. Widmann, Chairman, Philadelphia, Pa., W. S. Newcomet, Philadelphia, Pa., B. A. Hughes, Philadelphia, Pa.

*Representative on The American Board of Radiology:* Rollin H. Stevens, Detroit, Mich.

*Twenty-second Annual Meeting:* Atlantic City, N. J., June 7-8, 1937.

# EDITORIAL

## THE ANNUAL MEETING

WITH the approach of the end of summer and September our thoughts quite naturally turn to the meeting of the American Roentgen Ray Society. This year's meeting, the thirty-seventh in the Society's history, will be held at Cleveland on September 29 to October 2 at the Hotel Cleveland. As an indication of the quality and character of the meeting which is in store for the members of the Society and its guests one need only turn to the scientific program in this issue of the Journal which has been arranged by the President-elect, Dr. Waters, and his program committee. The organizers and officers of the American Roentgen Ray Society were fortunate in selecting September as the date of the annual meeting as this time ushers in the return of people from their vacations and scholars to their various colleges and also ushers in the return of mental activity which has had some respite during the summer vacation period. As a stimulus to this mental activity the annual meeting is a great adjuvant because it not only offers an opportunity for the members to present the work they have had in progress during the year but also an opportunity for an exchange of ideas which may act as a catalyzer in our scientific endeavors during the coming winter. Dr. Waters has arranged a program which should make an appeal to all members of the Society because of the breadth of its scientific import.

One of the outstanding features of the annual meeting is always the Caldwell Lecture which is to be given on Tuesday evening. This year's Caldwell lecturer will be Professor Robert A. Millikan who will talk on "High Energy Radiations and Their Uses." This lecture should prove of enormous interest to the members of the Society and its guests, and we ought to congratulate ourselves upon Dr. Millikan's acceptance of the invitation to deliver the Caldwell Lecture.

The place of the meeting, Cleveland, is a city accessible by all modes of travel and its central location offers an ideal meeting place. Then, too, the Local Committee of Arrangements under the chairmanship of Dr. B. H. Nichols has arranged a splendid program of entertainment which should be of added inducement to encourage a large attendance.

The time and the place of the meeting, the scientific program, and the scientific and commercial exhibits augur well for the 1936 meeting of the American Roentgen Ray Society to be one of the best that the Society has held.

Owing to the popularity of Cleveland as a convention city, it is earnestly urged upon the members of the Society that they make their hotel reservations at the earliest possible moment.

# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

*Items for this section solicited promptly after the events to which they refer.*

## MEETINGS OF ROENTGEN SOCIETIES*

### United States of America

**American Roentgen Ray Society**
*Secretary*, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa. Annual Meeting: Cleveland, Ohio, Sept. 29–Oct. 2, 1936.

**American College of Radiology**
*Secretary*, Dr. B. H. Orndoff, 2561 N. Clark Street, Chicago, Ill. Annual meeting, 1937: To be announced.

**Section on Radiology, American Medical Association**
*Secretary*, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting, 1937: To be announced.

**Radiological Society of North America**
*Secretary*, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N.Y. Annual meeting: Cincinnati, Ohio, Nov. 30–Dec. 4, 1936.

**Radiological Section, Baltimore City Medical Society**
*Secretary*, Dr. Howard H. Ashbury, Baltimore. Meets third Tuesday each month, September to May.

**Radiological Section, Connecticut State Medical Society**
*Secretary*, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets annually in May. Special meetings may be called by the Chairman.

**Radiological Section, Los Angeles County Medical Society**
*Secretary*, E. N. Liljedahl, Los Angeles, Calif. Meets on the second Wednesday of each month at the County Society Building.

**Radiological Section, Southern Medical Association**
*Secretary*, Dr. Roy G. Giles, Temple, Texas. Annual meeting, Baltimore, Md., Nov. 17–20, 1936.

**Brooklyn Roentgen Ray Society**
*Secretary*, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

**Buffalo Radiological Society**
*Secretary-Treasurer*, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

**Chicago Roentgen Society**
*Secretary*, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

**Cincinnati Radiological Society**
*Secretary*, Dr. H. G. Reineke, General Hospital Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

**Cleveland Radiological Society**
*Secretary*, Dr. North W. Shetter, 14600 Detroit Ave. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

**Denver Radiological Club**
*Secretary*, Dr. K. D. A. Allen, 452 Metropolitan Building, Denver, Colorado. Meets on any month having a fifth Monday.

**Detroit Roentgen Ray and Radium Society**
*Secretary*, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

**Florida State Radiological Society**
*Secretary*, Dr. Gerard Raap, Miami, Florida. Meetings held twice a year, May and November.

**Illinois Radiological Society**
*Secretary*, Dr. Cesare Gianturco, 602 W. University Ave., Urbana, Ill. Regular meetings held quarterly.

**Indiana Roentgen Society**
*Secretary*, Dr. C. C. Taylor, Indianapolis, Ind. Meeting held the second Sunday in May annually.

**Long Island Radiological Society**
*Secretary*, Dr. M. Dannenberg, 1464 Eastern Parkway, Brooklyn, N. Y. Meets on third Thursday of each month from October to May, at 8:30 P.M.

**Michigan Association of Roentgenologists**
*Secretary*, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing, Mich. Three meetings a year, Fall, Winter, and Spring.

**Milwaukee Roentgen Ray Society**
*Secretary*, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting designed by the president.

**Minnesota Radiological Society**
*Secretary*, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.

**Nebraska State Radiological Society**
*Secretary*, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday evening of each month.

**New England Roentgen Ray Society**
*Secretary*, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

**Radiological Society of New Jersey**
*Secretary*, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

**New York Roentgen Society**
*Secretary*, Dr. E. F. Merrill, 30 W. 59th St., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

**North Carolina Roentgen Ray Society**
*Secretary*, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

**Central New York Roentgen Ray Society**
*Secretary*, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse, N. Y. Three meetings a year—January, May, and November.

**Pacific Roentgen Club**
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

**Pennsylvania Radiological Society**
*Secretary*, Dr. L. E. Wurster, Williamsport, Pa. Next annual meeting June 5 and 6, 1936, Lycoming Hotel, Williamsport, Pa.

**Philadelphia Roentgen Ray Society**
*Secretary*, Dr. Thomas Loughery, Germantown Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

**Rochester Roentgen Ray Society, Rochester, N. Y.**
*Secretary*, Dr. Camp C. Thomas, 476 Lake Ave. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

**St. Louis Roentgen Ray Society**
*Secretary*, Dr. P. C. Schnoebelen, Missouri Bldg., St. Louis, Mo. Meets first week of each month. Time and place of meetings designated by president.

**South Carolina X-Ray Society**
*Secretary*, Dr. R. B. Taft, 105 Rutledge Ave., Charleston. Meets at time and place of South Carolina State Medical Association.

**Tennessee Radiological Society**
*Secretary*, Dr. F. B. Bogart, 311 Medical Arts Bldg.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
*Secretary-Treasurer*, Dr. J. H. Smith, Lubbock, Texas
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Department of Roentgenology Staff Meeting
*Secretary*, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich.
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Roentgen Club
*Secretary*, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis.
Meets monthly on last Thursday, October to April, Service Memorial Institute, at 4:30 P.M.

Virginia Roentgen Ray Club
*Secretary*, Dr. V. W. Archer, University Hospital, University, Va.
Meets annually in October.

### Cuba

Sociedad Cubana de Radiologia y Fisioterapia
*Secretary*, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

### British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
*Secretary*, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
*Secretary*, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
*Secretary*, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
*Secretary*, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

### Continental Europe

Belgian Society of Roentgenology
*Secretary*, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Española de Radiologia y Electrologia
*Secretary*, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
*Secretary*, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
*Permanent secretary*, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
*Secretary*, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
*Secretary*, Dr. G. Gatoschi, Str. Isvor 14–16, Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
*Secretaries*, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
*Secretaries*, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
*Secretaries*, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
*Secretary*, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
*Secretary*, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
*Secretary*, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6.30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

### Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

# SCIENTIFIC PROGRAM
# OF THE
# THIRTY-SEVENTH ANNUAL MEETING
## OF THE
## AMERICAN ROENTGEN RAY SOCIETY, SEPTEMBER 29–OCTOBER 2, 1936
## HOTEL CLEVELAND, CLEVELAND, OHIO

### Tuesday Morning, September 29, 1936

9:00 A.M.

Call to order, Fred M. Hodges, M.D., President.

Presentation of medals and certificates.

Installation of incoming President.

President's Address. Charles A. Waters, M.D.

9:30 A.M.

1. Roentgen-ray studies of the large bowel in infections with *Endamoeba histolytica* before, during and subsequent to treatment. Joseph C. Bell, M.D., Louisville, Ky. (15 min.)
   Discussion (5 min.) to be opened by Harry M. Weber, M.D., Rochester, Minn.

2. Tuberculosis of the gastrointestinal tract. Harry M. Weber, M.D., and B. R. Kirklin, M.D., Rochester, Minn. (15 min.)
   Discussion (5 min.) to be opened by Raymond C. McKay, M.D., Cleveland, Ohio (by invitation).

3. Roentgenographic observation of the biliary ducts during and following operation by cholangiography. Howard B. Hunt, M.D. (by invitation), Russell R. Best, M.D. (by invitation) and Frederick N. Hicken, M.D. (by invitation), Omaha, Neb. (15 min.)
   Discussion (5 min.) to be opened by Harry G. Sloan, M.D., Cleveland, Ohio (by invitation).

4. The influence of extrabiliary diseases and other conditions on the function of the gallbladder as related to cholecystography. Byrl R. Kirklin, M.D., and C. A. Good, M.D. (by invitation), Rochester, Minn. (15 min.)
   Discussion (5 min.) to be opened by Hollis E. Potter, M.D., Chicago, Ill.

5. Roentgen-ray studies of diseases of the liver and spleen. Charles L. Martin, M.D., Dallas, Texas. (15 min.)
   Discussion (5 min.) to be opened by Arthur W. Erskine, M.D., Cedar Rapids, Iowa.

Adjournment at 11:30 A.M. for special study of Scientific Exhibits.

### Tuesday Afternoon, September 29, 1936

2:00 P.M.

1. The clinical aspects of adenomas of the pituitary body. Elliott C. Cutler, M.D. (by invitation), and Max T. Schnitker, M.D. (by invitation), Boston, Mass. (15 min.)
   Discussion (5 min.) to be opened by W. James Gardner, M.D., Cleveland, Ohio (by invitation).

2. The place of irradiation in the treatment of pituitary adenomas. W. W. Vaughan, M.D. (by invitation), Boston, Mass. (15 min.)
   Discussion (5 min.) to be opened by Cornelius G. Dyke, M.D., New York City.

3. The effect of irradiation on pituitary basophilism (Cushing's syndrome). Merrill C. Sosman, M.D., Boston, Mass. (15 min.)
   Discussion (5 min.) to be opened by Eugene P. Pendergrass, M.D., Philadelphia, Pa.

4. The effect of irradiation on gliomas of the brain. Charles H. Frazier, M.D. (by invitation), Bernard J. Alpers, M.D. (by invitation), Eugene P. Pendergrass,

M.D., and George W. Chamberlin, M.D. (by invitation), Philadelphia, Pa. (15 min.)

Discussion (5 min.) to be opened by W. James Gardner, M.D., Cleveland, Ohio (by invitation).

5. The effects of irradiation on the normal blood cells as determined by the blood count. Karl Kornblum, M.D., Fred Boerner, M.D. (by invitation), and Samuel G. Henderson, M.D. (by invitation), Philadelphia, Pa. (15 min.)

Discussion (5 min.) to be opened by Russell L. Haden, M.D., Cleveland, Ohio (by invitation), and Wright Clarkson, M.D., St. Petersburg, Va.

6. The care of the cancer patient. Elwood E. Downs, M.D., Hoke Wammock, M.D. (by invitation), and R. Townsend Artman, M.D. (by invitation), Philadelphia, Pa. (15 min.)

Discussion (5 min.) to be opened by Kenneth D. A. Allen, M.D., Denver, Colo.

Tuesday Evening, September 29, 1936

8:30 P.M.

Introductory Remarks. W. Edward Chamberlain, M.D., Philadelphia, Pa.

The Caldwell Lecture. "High Energy Radiations and Their Uses." Professor Robert A. Millikan, Pasadena, Calif.

Wednesday Morning

September 30, 1936

9:00 A.M.

1. Hodgkin's disease and allied conditions of bone. Richard Dresser, M.D., and Jack Spencer, M.D. (by invitation), Boston, Mass. (15 min.)

Discussion (5 min.) to be opened by Ross Golden, M.D., New York City.

2. The generalized form of "Boeck's sarcoid." Warfield T. Longcope, M.D. (by invitation), and John W. Pierson, M.D., Baltimore, Md. (15 min.)

Discussion (5 min.) to be opened by George W. Holmes, M.D., Boston, Mass.

3. Bone lesions induced by anterior pituitary and parathyroid extracts (carbohydrate disturbances associated with bone lesions). Lawrence Reynolds, M.D., R. C. Moehlig, M.D. (by invitation), and Sidney Adler, M.D. (by invitation), Detroit, Mich. (15 min.)

Discussion (5 min.) to be opened by Howard T. Karsner, M.D., Cleveland, Ohio (by invitation).

4. Osteoporosis circumscripta of the skull and Paget's disease. Fifteen new cases and a review of the literature. Haig H. Kasabach, M.D., and Alexander B. Gutman, M.D., New York City (15 min.)

Discussion (5 min.) to be opened by Sherwood Moore, M.D., St. Louis, Mo.

5. The etiology of Paget's disease. E. P. Corson White, M.D. (by invitation), Philadelphia, Pa., and Ralph S. Bromer, M.D., Bryn Mawr, Pa. (15 min.)

Discussion (5 min.) to be opened by Merrill C. Sosman, M.D., Boston, Mass., and Howard T. Karsner, M.D., Cleveland, Ohio (by invitation).

Adjournment at 11:30 A.M. for special study of Scientific Exhibits.

Wednesday Afternoon

September 30, 1936

2:00 P.M.

1. The production of supervoltage roentgen rays by means of the Van de Graaff generator. Richard Dresser, M.D., Boston, Mass. (15 min.)

Discussion (5 min.) to be opened by Lauriston S. Taylor, Ph.D., Washington, D.C.

2. Co-ordination of physical and biologic dosage in high voltage and supervoltage roentgen therapy. Traian Leucutia, M.D., and K. E. Corrigan, Ph.D. (by invitation), Detroit, Mich. (15 min.)

Discussion (5 min.) to be opened by Lauriston S. Taylor, Ph.D., Washington, D.C.

3. Dosage measurements on six 400 kilovolt roentgen therapy machines. Otto Glasser, Ph.D., Cleveland, Ohio. (15 min.)
   Discussion (5 min.) to be opened by Lauriston S. Taylor, Ph.D., Washington, D.C.

4. Biophysical considerations relating to the radiological treatment of cancer of the larynx. Gioacchino Failla, D.Sc., New York City. (15 min.)
   Discussion (5 min.) to be opened by K. E. Corrigan, Ph.D., Detroit, Mich. (by invitation), and Lauriston S. Taylor, Ph.D., Washington, D.C.

5. The practical measurement of tissue dosage in x-ray therapy in terms of a fundamental unit. Edith H. Quimby, M.A., L. D. Marinelli, M.D. (by invitation), and Joseph Farrow, M.D. (by invitation), New York City. (15 min.)
   Discussion (5 min.) to be opened by Lauriston S. Taylor, Ph.D., Washington, D.C.

6. Prolonged low intensity irradiation. Ira I. Kaplan, B.Sc., M.D., and Sidney Rubenfeld, B.Sc., M.D. (by invitation), New York City. (15 min.)
   Discussion (5 min.) to be opened by Eugene P. Pendergrass, M.D., Philadelphia, Pa.

7. Fracture of the femoral neck following irradiation. Harold W. Jacox, M.D., Pittsburgh, Pa., Robert G. Dalby, M.D. (by invitation), Ann Arbor, Mich. (deceased), and Norman F. Miller, M.D. (by invitation), Ann Arbor, Mich. (15 min.)
   Discussion (5 min.) to be opened by William McDowell Doughty, M.D. Cincinnati, Ohio.

### Wednesday Evening
### September 30, 1936

7:00 P.M. *Stag Dinner.*

### Thursday Morning, October 1, 1936

9:00 A.M.

1. Hernia of the mediastinum. Howard P. Doub, M.D., and Horace C. Jones, M.D. (by invitation), Detroit, Mich. (15 min.)
   Discussion (5 min.) to be opened by Claude Beck, M.D., Cleveland, Ohio (by invitation).

2. Acute infections of the mediastinum. Clinical manifestations, diagnosis, operative indications and technique; results. Harold Neuhof, M.D. (by invitation), New York City. (15 min.)

3. Acute infections of the mediastinum. Classification, pathogenesis, pathology, roentgen features. Coleman B. Rabin, M.D. (by invitation), New York City. (15 min.)
   Discussion of papers Nos. 2 and 3 (5 min.) to be opened by Claude Beck, M.D., Cleveland, Ohio (by invitation).

4. Roentgen kymographic studies of pulmonary lesions. Wendell G. Scott, M.D. (by invitation), and Sherwood Moore, M.D., St. Louis, Mo. (15 min.)
   Discussion (5 min.) to be opened by Sydney Johnson, M.D., Louisville, Ky. (by invitation).

5. The roentgenological diagnosis of pericardial adhesions (adhesive pericarditis) and encapsulated pericardial effusions. Eugene Freedman, M.D. (by invitation), Cleveland, Ohio. (15 min.)
   Discussion (5 min.) to be opened by Whitmer B. Firor, M.D., Baltimore, Md.

Adjournment at 11:30 A.M. for special study of Scientific Exhibits.

### Thursday Afternoon, October 1, 1936

2:00 P.M.

1. The physiologic consideration of ileus. Alton Ochsner, M.D. (by invitation), New Orleans, La. (15 min.)
   Discussion (5 min.) to be opened by LeRoy Sante, M.D., St. Louis, Mo.

2. The rôle of the sex hormones in the radiation treatment of menstrual disorders. Milton Friedman, M.D. (by invitation) and Rita Finkler, M.D. (by invitation), New York City. (15 min.)
   Discussion (5 min.) to be opened by Charles F. Geschickter, M.D., Baltimore, Md. (by invitation), and E. Perry McCullagh, M.D., Cleveland, Ohio (by invitation).

3. Endocrines and irradiation in experimental hypertrophy of the prostate. Charles F. Geschickter, M.D. (by invitation), Baltimore, Md. (15 min.)
   Discussion (5 min.) to be opened by E. Perry McCullagh, M.D., Cleveland, Ohio (by invitation).

4. Pituitary diseases and their response to roentgen therapy. Ursus V. Portmann, M.D., and E. Perry McCullagh, M.D. (by invitation), Cleveland, Ohio. (15 min.)
   Discussion (5 min.) to be opened by Charles F. Geschickter, M.D., Baltimore, Md. (by invitation).

5. Roentgen therapy of infections and inflammations. Willis F. Manges, M.D., and R. Manges Smith, M.D. (by invitation), Philadelphia, Pa. (15 min.)
   Discussion (5 min.) to be opened by Fred M. Hodges, M.D., Richmond, Va., and Roy G. Giles, M.D., Temple, Texas.

6. The treatment of epithelioma in the region of the ear. (With lantern slide demonstration and with a scientific exhibit.) George E. Pfahler, M.D., Sc.D., and Jacob H. Vastine, M.D., Philadelphia, Pa. (15 min.)
   Discussion (5 min.) to be opened by Edwin A. Merritt, M.D., Washington, D.C.

7. Radiotherapy for endothelioma (endothelial myeloma) of bone. Arthur U. Desjardins, M.D., H. W. Meyerding, M.D. (by invitation), and Eugene T. Leddy, M.D., Rochester, Minn. (15 min.)
   Discussion (5 min.) to be opened by Charles F. Geschickter, M.D., Baltimore, Md. (by invitation).

4.30 P.M. *Executive Session.*

THURSDAY EVENING, OCTOBER 1, 1936

7:00 P.M. *Banquet.*

FRIDAY MORNING, OCTOBER 2, 1936

9:00 A.M.

1. Planigraphy and tomography: The roentgenographic representation of plane sections of solid objects. J. Robert Andrews, M.D. (by invitation), Cleveland, Ohio. (15 min.)
   Discussion (5 min.) to be opened by W. Edward Chamberlain, M.D., Philadelphia, Pa.

2. A preliminary report on cine-fluorography. William H. Stewart, M.D., William J. Hoffman, M.D., (by invitation), and F. H. Chiselin, M.D. (by invitation), New York City. (15 min.)
   Discussion (5 min.) to be opened by Lewis Gregory Cole, M.D., New York City.

3. Roentgen observations on obliterative bronchitis. Leo G. Rigler, M.D., Minneapolis, Minn. (15 min.)
   Discussion (5 min.) to be opened by Henry Kennon Dunham, M.D., Cincinnati, Ohio.

4. Roentgen evidence of the behavior of human lung in recent tuberculous infections. Kenneth D. A. Allen, M.D., Denver, Colo. (15 min.)
   Discussion (5 min.) to be opened by Henry Kennon Dunham, M.D., Cincinnati, Ohio.

5. The oblique projection of the thorax: An anatomic and roentgenologic study. Carleton B. Peirce, A.B., M.S., M.D., and Bruce Stocking, M.D. (by invitation), Ann Arbor, Mich. (15 min.)
   Discussion (5 min.) to be opened by John W. Pierson, M.D., Baltimore, Md.

6. Congenital or infantile dislocation of the hips. Edward C. Vogt, M.D., Boston, Mass. (15 min.)
   Discussion (5 min.) to be opened by Theodore A. Willis, M.D., Cleveland, Ohio (by invitation).
7. The present status of roentgen-ray pelvimetry and cephalometry. Paul C. Hodges, M.D., Chicago, Ill. (15 min.)
   Discussion (5 min.) to be opened by Henry J. Walton, M.D., Baltimore, Md.

FRIDAY AFTERNOON, OCTOBER 2, 1936

2:00 P.M.

1. A roentgenologic criterion of dermoid Cyst. Dallas B. Phemister, M.D. (by invitation), Chicago, Ill., William B. Steen, M.D. (by invitation), Chicago, Ill., and John C. Volderauer, M.D. (by invitation), Ann Arbor, Mich. (15 min.)
   Discussion (5 min.) to be opened by Howard C. Doub, M.D., Detroit, Mich.
2. Lesions of the diaphragm. Report of 100 cases. Edward L. Jenkinson, M.D., and E. W. Roberts, M.D. (by invitation), Chicago, Ill. (15 min.)
   Discussion (5 min.) to be opened by William H. Stewart, M.D., New York City.
3. Clinical and roentgenological study of low back pain with sciatic radiation. A. Clinical aspects. Carl E. Badgley, M.D. (by invitation), Theodore W. Bywaters, M.D. (by invitation), and Robert E. Hastings, M.D. (by invitation), Ann Arbor, Mich. (15 min.)
   Discussion (5 min.) to be opened by Theodore A. Willis, M.D., Cleveland, Ohio (by invitation).
4. Clinical and roentgenological study of low back pain with sciatic radiation. B. Roentgenological aspects. Fred Jenner Hodges, M.D., and Willis S. Peck, M.D. (by invitation), Ann Arbor, Mich. (15 min.)
   Discussion (5 min.) to be opened by Theodore A. Willis, M.D., Cleveland, Ohio (by invitation).
5. The lipiodo-diagnosis of rupture of the intervertebral discs into the spinal canal (with particular reference to those lesions simulating sciatica and low back strain). Aubrey O. Hampton, M.D., and J. Maurice Robinson, M.D. (by invitation), Boston, Mass. (15 min.)
   Discussion (5 min.) to be opened by Wallace Duncan, M.D., Cleveland, Ohio
6. Determination of gamma-ray activity of thorotrast in liver patients. Robert B. Taft, M.D., and Hillyer Rudisill, M.D., Charleston, S.C. (15 min.)
   Discussion (5 min.) to be opened by Thomas A. Groover, M.D., Washington, D.C.
7. Roentgen therapy by the method of Chaoul. Eugene P. Pendergrass, M.D., Philadelphia, Pa. (15 min.)

FINAL ADJOURNMENT

# CLEVELAND

## MEETING PLACE FOR 1936

CLEVELAND was an isolated trading post on the Western Reserve frontier when Moses Cleaveland laid out the Public Square in 1796. Today, it is the metropolis of Ohio—the capital of a great trade empire—the home of more than a million people.

Towering skyscrapers, busy streets, huge industrial plants, charming homes—these surround the spot where a little cluster of log cabins nestled in a small clearing carved out of the wilderness. Cleveland's Public Square has always been the hub of its activities. But the Connecticut Land Company purchased it in 1795 for $1.76. Today, a reasonable sale price would be $20,000,000.

Moses Cleaveland chose his site because it

promised splendid trading and commercial possibilities. His selection was a fortunate one. Cleveland's location on the southern shore of Lake Erie is the logical meeting place for iron ore, coal and limestone. The result has been to make the city a world power in industry and commerce.

Lake Erie is a busy thoroughfare during the navigation season. The great freighters passing to and fro are vivid pictures of the colorful traditions of the lake. The efficient equipment used at the docks to load and unload the valuable cargoes affords many an interesting and educational hour to the visitor.

*Lake Port Development.* The "Walk-in-the-Water," Lake Erie's first steamboat, opened Cleveland's career as a lake port when it made its first trip from Buffalo in August, 1818. Soon the almost daily arrival of boatloads of 500 persons became a common sight. Many of these adventurers recognized the future of the little community and went no farther inland. Thus, the city's population steadily grew.

The immense lake traffic of today was born when the first cargo of iron ore from the Lake Superior region entered the harbor in 1852. A view of the fourteen miles of lake front protected by the breakwater five and three-fourths miles long and the harbor amply supplied with docks both along the lake and the Cuyahoga River banks makes it easy to understand how Cleveland meets the demands of its ever-increasing lake business.

Far-seeing business men soon realized Cleveland's advantages. Manufacturing sprang up. These industries grew and more were attracted. Today, 2,500 industrial plants are located in the community and their aggregate yearly payroll is in excess of two hundred million dollars. The visitor can well spend several interesting days visiting the city's plants.

The Medical Library, University Hospitals, and the Western Reserve Medical School

Cleveland is a natural transportation center. It is easy to reach by rail, water, air or motor. Trunk railroad lines, interurban, motor coach and air lines enter the city from all major travel centers. The new Union Passenger Terminal is one of the world's finest. This great building and its companion group have been called a "City within a City." Only through inspecting them can their magnitude be realized.

*City of Surprises.* Building construction has made rapid strides in Cleveland during the past few years. It is a city of surprises for those

who have not seen it recently. Its huge office buildings, its skyscrapers, its Public Auditorium and other developments have attracted the attention of the whole nation.

Through all of Cleveland's progress runs the spirit of the early trail blazers who did their work so well that they exceeded the fondest expectations of their leader, Moses Cleaveland, who reported to his employers that he believed, and the new Municipal Stadium. The Mall with its beautiful landscaping presents an unequaled example of civic accomplishment.

*Community Fund.* The Community Fund, used today by every city of consequence in the United States, was perfected in Cleveland. Through this centralization of social welfare financing, the amount of money realized for these important activities has been greatly

Mt. Sinai Hospital

"the child is now born who may live to see that place as large as old Wyndham." Today, the population of Wyndham is slightly more than 14,000.

### CITY WITH A CIVIC HEART

Cleveland's Mall is one of the most ambitious undertakings ever attempted. This plan of grouping public buildings around a spacious 17 acre downtown garden spot represents an investment of more than $40,000,000. The Mall, which overlooks Lake Erie and extends into the heart of the business district, is made up of seven great buildings, America's best equipped convention plant, the $15,000,000 Public Auditorium, the Federal Building, the Public Library, the new Board of Education Building, City Hall, Cuyahoga County Court House, increased. Citizens pledged $3,037,696.87 for Cleveland's 1934 welfare and relief needs. There were 445,295 donors. Before the Fund was established, 5,000 givers bore the annual burden. The Community Fund assists 100 local agencies in their welfare and relief work.

*Chamber of Commerce.* Cleveland's Chamber of Commerce, since its organization in 1848 as the Cleveland Board of Trade, has been unusually active in Cleveland's progress. Its members represent every phase of the city's life, making its various undertakings practically indicative of the wishes of the community as a whole.

The Chamber of Commerce Transportation Bureau is credited with being the best organized in America. Its Foreign Trade Committee has materially aided manufacturers through its

Statue of Moses Cleaveland. This statue of Moses Cleaveland in Cleveland's Public Square stands as a memorial to the intrepid surveyor and veteran of the Revolutionary War, who founded the city in 1796. He was born in 1754 in Canterbury, Conn., and died in 1806. The city was named after him, with the omission of a superfluous vowel, said to have been dropped originally to make type fit in a newspaper title, in 1830.

export research. The Industrial Development Committee is active in commercial and industrial progress. All of the many other departments are equally valuable.

*Cleveland's Progressiveness.* Cleveland's progressiveness in political thought and civic welfare is due largely to its diversified population. The inherited conservatism of the descendents of the city's founders is balanced by the restless liberalism which brought from the Old World the many immigrants attracted to the city by its strategic location and industrial possibilities.

An individual who left a most lasting impression upon Cleveland was Tom L. Johnson, its beloved mayor for eight years late in the nineteenth century. Always fighting unselfishly for the best interests of the community he inaugurated many innovations which have been important factors in municipal progress throughout the country.

The lasting impression that Tom L. Johnson made upon the City of Cleveland is illustrated by the inscription which appears on his statue in the Public Square:

He found us striving each his selfish part
He left a city with a civic heart.

### INDUSTRIAL CAPITAL

Cleveland is a city of diversified industry today but the backbone of its development has been its convenient location to the rich Lake Superior iron ore region and the coal and limestone fields of Pennsylvania and Ohio. This happy choice of location has made Cleveland the capital of a great trade empire.

The 2,500 plants in Cleveland normally employ 140,000 wage earners and more than a billion dollars worth of products are manufactured annually. At least two-thirds of the nation's industries are represented.

*Steel.* Iron and steel, of course, have been Cleveland's major industries since 1828 when the first smelter was established. From this little plant with a weekly output of 20 tons has developed the great industry of today when Cleveland's smelters have a capacity of three million tons of pig iron annually.

A vast fleet of boats with capacities as high as 12,000 tons keep Cleveland supplied with ore. Huge unloaders take the ore from the ships almost a carload at a time. Mammoth

Cleveland Clinic Hospital

cranes dump it in storage piles which soon become small mountains. From these great mounds, the ore goes to the blast furnaces some of which produce as much as 600 tons a day. One of Cleveland's plants has a capacity of more than 700,000 tons of steel products a year.

Steel, though the leader, is only one of many industries in Cleveland. The city leads the world in the production of wire nails, bolts and screws, malleable castings and heavy machinery. It is one of the nation's largest hardware centers. The multigraph machine used in your office was made in Cleveland. Only one city in the United States produces more sewing machines. All kinds of products from huge hoisting and conveying machinery to toys and small novelties are produced in the city's plants.

Foundry and machine shop products manufactured annually are valued at $127,000,000. The yearly output of motor vehicles, bodies and parts is valued at more than $150,000,000. More than $98,000,000 worth of iron and steel mill products are manufactured each year.

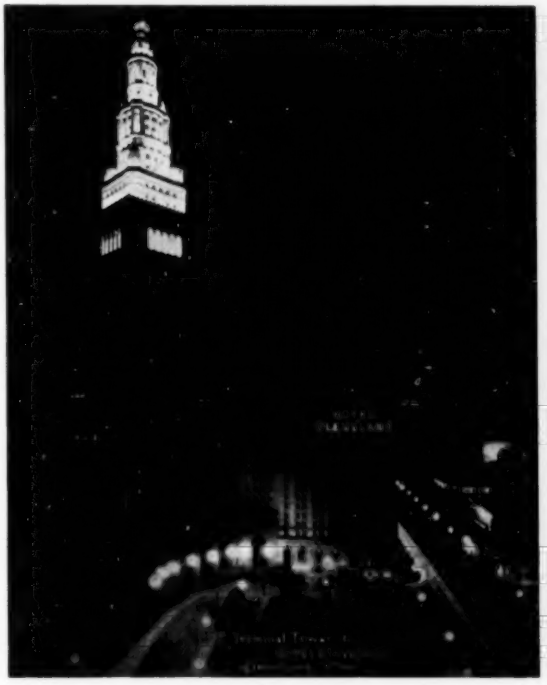
*Diversified Industries.* Cleveland is a leader in the production of paint and varnish. Two of the world's largest paint companies maintain administrative offices and plants in the city. This industry's 43 factories in Cleveland have an aggregate output of $36,000,000 while the output of refined oils totals more than a billion gallons.

The ready-made clothing industry in Cleveland takes high rank. More than 5,600 persons are employed to make $30,000,000 worth of men's clothing each year. Women's garments manufactured each year are valued at $28,000,000. More than $12,000,000 worth of knit goods are produced annually.

The annual output of electrical machinery, apparatus and supplies is valued at more than $60,000,000

The brick and tile output in Cleveland has a value of $60,000,000 a year. Two hundred and fifty million bricks and 300,000 tons of tile are manufactured annually.

Nela Park, the headquarters of the National Lamp Works of the General Electric Company, is located at Cleveland. The Park's 75 acres, noted for their unusual beauty, stand as a monument to scientific research in modern industry. Ten thousand persons visit Nela Park every year to inspect the extensive exhibits and fascinating demonstrations designed especially for the public.



Terminal Tower at Night—Hotel Cleveland

INTERNATIONAL TRADING CENTER

*Exports.* There is hardly a point on the earth where Cleveland-made goods will not be found or a country whose goods are not imported to Cleveland.

Australians drive motor trucks made in Cleveland. Blast furnace equipment perfected in this great industrial center is shipped to China. The mines of South Africa, the Andes, Bolivia and Chile are equipped with wire screens made in Cleveland. Cleveland sells letter duplicating equipment to England, paint to Italy and twist drills to China. Japan buys automatic screw machines created in America's sixth city. Entire Russian cities have been designed and built by Cleveland engineering firms.

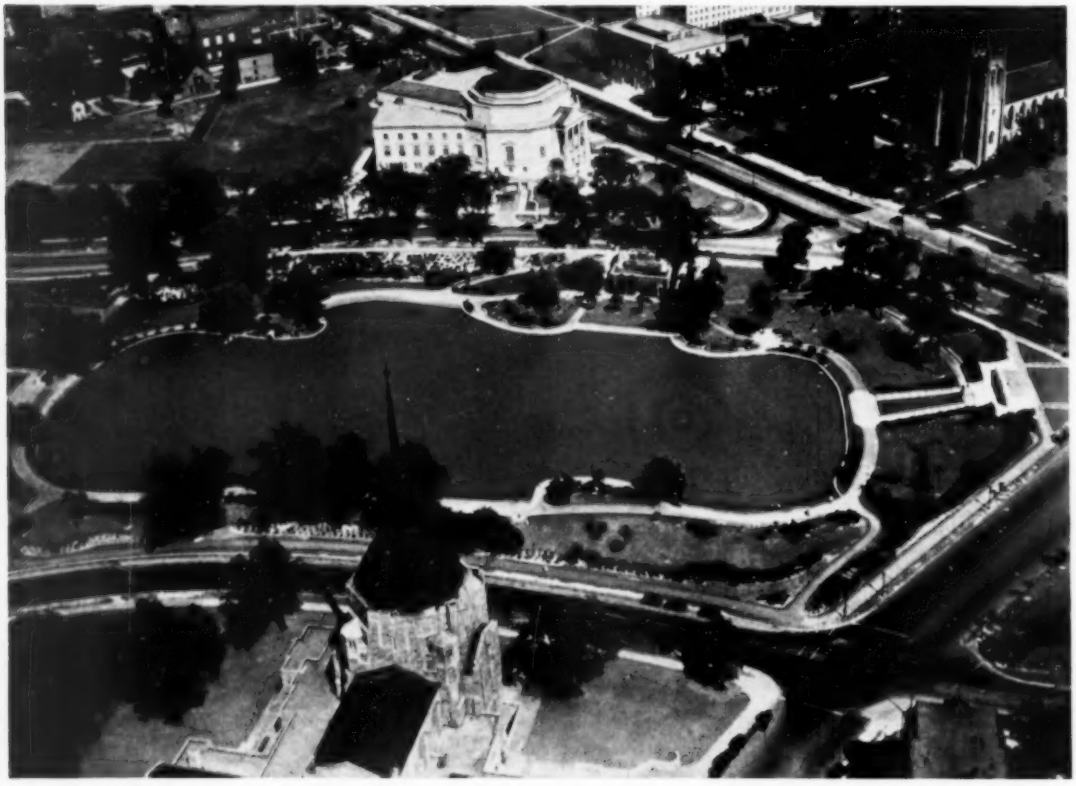
In recent years a market for lubricating oils has been developed in Northern Europe while petroleum in large quantities is exported to Japan. Cleveland-built tractors cultivate sugar cane in Mauritius and in the Fiji Islands and haul timber in the heart of the Belgian Congo. Sir Hubert Wilkins used tractors made in Cleveland on his Antarctic expedition for hauling planes from their hangars to suitable taking-off places.

Printing presses are shipped to every part of the world. Coal and ore handling machinery is

sent to France and Belgium. Railway cars and locomotives are made in Cleveland for the Dutch East Indies, India, Java and Sumatra. Turret lathes are sold wherever there are railroad shops and dental instruments have a market wherever dentistry is practiced. Telescopes made in Cleveland have gained world renown.

breakwater five and three-fourths miles long. The harbor has a spacious entrance and extensive dockage for passenger and freight service. The Cuyahoga River, emptying into the western end of the harbor, is lined with docks adjacent to which are furnaces, factories and lumber yards.

In addition to its water traffic, Cleveland's



A lagoon in Wade Park from the air. Severance Hall, home of the Cleveland Symphony Orchestra, is seen in the central background. Parts of the campuses of Western Reserve University and Case School of Applied Science may also be seen in the extreme background.

Cleveland's gross annual export trade exceeds $200,000,000 or 1,500,000 ships tons. Four hundred Cleveland manufacturers produce 3000 different lines of commodities. Cleveland's import business equals its export trade with $200,000,000 worth of products shipped into the city each year from all parts of the world.

It can readily be seen that Cleveland's docks are busy places. The tonnage handled annually is greater than that of Liverpool and greater than that handled by all of the ports of France combined.

*Transportation.* Cleveland has 14.2 miles of Lake frontage. Its harbor is protected by a

yearly receipts include 15,000,000 tons of freight by rail. Ten million tons are forwarded from Cleveland by rail annually. Every year, railroads bring 8,500,000 tons of coal and coke to the city. A great lake port and a busy railroad center, Cleveland becomes more and more important as an international trading center each year.

### EDUCATION

Cleveland is an outstanding cultural center. With its two great universities, its high-ranking technical school, its 300 public and parochial schools, its numerous colleges and preparatory schools and its art and music schools,

Cleveland is one of the nation's educational leaders.

*Universities and Colleges.* Practically every branch of education can be pursued at Western Reserve University, one of Ohio's oldest collegiate institutions. Nearly 15,000 students daily attend classes at the Mather College for Women, Adelbert College, the Schools of Medicine, Law, Dentistry, Pharmacy, Nursing, Applied Social Sciences, Library Science, Education, Architecture, the Graduate school and Cleveland College, the University's downtown branch.

Western Reserve's Schools of Medicine, Dentistry, Pharmacy and Nursing are affiliated with the University Hospitals Group. This great medical center on the University campus has placed the city among the world's leaders in medical science. The group, which represents an investment of more than $13,000,000, includes the School of Medicine, Babies' and Children's Hospital, Maternity Hospital, Lakeside Hospital, Leonard C. Hanna House, Nurses' Dormitory and the Institute of Pathology. Rainbow Hospital in South Euclid is part of the group. Associated with the group is the Allen Memorial Medical Library of the Medical Library Association.

Case School of Applied Science, adjoining the campus of Western Reserve, is one of the nation's best engineering schools. Case has an enrollment of 750 students in civil, mechanical, electrical, mining, metallurgical and chemical engineering courses. The two institutions occupy high ground overlooking the southern end of Wade Park, one of the most beautiful spots in Cleveland.

Terminal Tower Development from West

John Carroll University lays special emphasis on the classics and scientific studies. One of the interesting features of the institution is the seismological laboratory, equipped with three large instruments, the largest of which contains records of practically every tremor observed in the earth's surface in the last thirty years.

*Cooperative System.* The Cleveland Conference for Educational Cooperation, participated in by eighteen of the city's institutions, has aided materially the rapid development of Cleveland as a cultural center.

The Library of the Western Reserve Historical Museum is a research laboratory for

students at Western Reserve University. Students at the School of Art sketch and study design at the Museum of Art. The School of Education, operated jointly by the Board of Education and Western Reserve University, trains teachers for the city's public schools system.

Cleveland College on the Public Square is the downtown unit of Western Reserve University and Case School of Applied Science. Day and evening classes are conducted, the principal function of the College being adult education for those who are employed in the daytime and have only their evenings to devote to study. The College utilizes the laboratories of both Case and Western Reserve.

The Museum of Art admits children free at all times, maintains a children's museum and gives lessons to public school children. The Museum cooperates with the School of Education through courses for public school teachers and offers lectures for Western Reserve students. The Museum also sends special art exhibits to the city schools for class room study.

The Board of Education maintains a teacher at the Museum of Natural History for the instruction of visiting classes. Lectures are given to thousands of school children each year.

*Museum of Art.* The Cleveland Museum of Art is one of the most beautiful museum buildings in America. Its equipment for handling and preserving its treasures has no superior. Through its cooperation with the city's schools and colleges, the Museum has become an essential factor in the educational life of Cleveland.

The Museum's exhibits have been selected for their high quality and the collections are made up of the finest objects procurable and chosen with definite regard for their educational value.

Cleveland Museum of Art

In the work of teaching the appreciation of beauty and art, lectures, published articles and class talks are used. Classes are arranged for students of all ages. More than 300,000 persons visit the Museum annually, 70,000 of them being school children who receive art instruction. Classes for adults draw 27,000 each year.

*Museum of Natural History.* The Museum of Natural History has displays of Ohio birds, specimens of fossil fishes, 400,000 years old, insects, African, Indian and Eskimo material and a number of natural habitat groups. One of the most interesting collections in the Museum is from the Blossom expedition to the South Atlantic Ocean in 1925–1926. The schooner

Blossom during its two and a half year cruise of exploration crossed the Atlantic four times, traveled 20,000 miles, touching three continents, and scores of little known, scientifically rich islands.

*Public Library.* The Cleveland Public Library is an outstanding educational feature of this city. Nine and one-half million books are borrowed from the library annually, one million educational volumes are circulated each year through its county library department. Eight million visitors enter the library each year for reading and reference.

Each week the bulletin board in the main Library, a $5,000,000 building on the Mall, records current events with appropriate reading suggestions. A business information bureau is operated and monthly bulletins listing sources of business information are issued. The Library also has a reference service and is a clearing house for business data.

*Cleveland Orchestra.* An institution which has done much to carry the story of Cleveland's educational and cultural progress to the rest of the world is the Cleveland Orchestra, one of America's finest symphony orchestras. This famous musical organization has played concerts in more than half the states in the Union and in Cuba and Canada.

Severance Hall, the new $2,500,000 home of the orchestra, at University Circle, is an important addition to the cultural center adjacent to the campus of Western Reserve University which donated the land for the building. The building is the gift of John Long Severance. The generosity of Cleveland music lovers makes possible the maintenance and endowment of the Cleveland Orchestra.

City Hospital

The Cleveland Orchestra plays an important part in the community's music education. About twenty children's concerts are given each season attended by more than thirty thousand children. These concerts, arranged in cooperation with the Board of Education, make a unique climax to public school lessons in music appreciation. The supervisor of music issues a special study leaflet, based on the music played at the children's concerts, which is used as a text, with gramophone records, in regular class work in certain elementary grades. Through this instruction thousands of children are benefited. That the Cleveland public schools rank with two of this country's great universities as experimental ground in music edu-

cation is largely the result of stimulation given music in Cleveland by the Cleveland Orchestra.

### MUNICIPAL ACHIEVEMENTS

Warrensville Farm for charitable and corrective purposes is a striking example of the spirit of Cleveland citizens. This great experiment which has brought many students of social welfare to Cleveland occupies 2,000 acres of high ground some seven miles from the city.

Here tuberculous patients are cared for. Aged couples are enabled to spend their last years together in a cottage built expressly for that purpose. Inmates of the House of Correction are taught useful occupations—in the shops in winter and in the farm fields in summer. Children with symptoms of tuberculosis attend open air classes in their own tent colony. The institution's own dairy supplies the patients with high-grade milk and butter. Many prize-winning cows will be found among the farm's large herd.

*Street Railway System.* Cleveland's street car service has been declared the best of any city in the United States by the world's greatest engineers and experts in municipal affairs. Transportation facilities have always met the increasing demands of a tremendous growth in population.

Cleveland's street railway system dates back to September 10, 1860, when 9 six-passenger horse cars were put into operation. During the first year only a few thousand persons rode the cars. Today there are 1,302 55-passenger cars in Cleveland using 407 miles of track. Twenty-eight articulated trains with 100 seating capacity are also in use and 150 single deck motor buses. Four thousand five hundred employees are required to operate the lines. The "Taylor" Franchise, a service at cost agreement, under which the street railway system has been operating since 1910, has drawn the attention of street railway experts throughout the nation. Under this plan the company is allowed 6 per cent return of its capital and fares are raised or lowered depending on the condition of the interest fund.

*Airport.* Cleveland's 1,000-acre airport is one of the largest municipally owned aviation fields in the country. The Eastern Division headquarters of the transcontinental day and night mail route is located on the main field. Passenger and express service is available to every point in this country. The second field is occupied by the Ohio National Guard flying unit.

The Department of Commerce has given the airport an A 1 A rating. The average ship movement is 3,500 per month. The port has twelve hangars. Service is available for all types of ships and motors.

A visit to the Airport at night is most interesting. Planes may be seen landing and leaving by the light of a 500,000,000 candle power flood light.

### THE CONVENTION CENTER

Cleveland's unexcelled facilities, its valuable experience through years of serving large and small conventions and its location make it an ideal meeting place.

Tempered in summer and winter by the lake breezes, the climate is always pleasantly moderate.

*Accessibility.* With half of the population of the United States and Canada living within an overnight's ride, maximum attendance is a regular report at Cleveland conventions. Every means of transportation—air, water, motor, rail—is available to bring you to the city.

During the lake navigation and air travel season it is particularly pleasant to make the trip by steamer or plane. All air and water schedules are synchronized with railroad schedules to and from all important centers so that the journey always requires the minimum of time and effort.

*Splendid Hotels.* Cleveland's hotel accommodations for its many convention visitors are splendid. Six hotels alone have 4,500 rooms—each with private bath. Designed for conventions, modern, and well equipped, these hotels assist materially in making Cleveland conventions successful. Numerous assembly, banquet and conference rooms are always available. Aside from the hotels mentioned above, there are many other beautiful hotels which make it possible to house the country's largest conventions.

An important feature in the larger hotels is the location of the meeting rooms. None of these are located higher than the mezzanine floor relieving the convention visitor of the annoyance of congestion at elevators. Hotel managers welcome conventions and strive in every way to cooperate with convention officials and committees. A strict price policy is adhered to and neither room rates nor restaurant charges are ever increased regardless of demand. The desire on the part of the hotels to please their guests has been one of the out-

standing reasons why Cleveland has built up so enviable a reputation as a convention city.

*World's Finest Auditorium.* When convention expositions require unusually complete facilities, Cleveland Public Hall is chosen. This $15,000,000 plant is the finest and most serviceable municipal auditorium in the country. Its range of service is practically unlimited. Sixteen events can be held simultaneously and without interference.

The huge Main Auditorium seats 12,500 persons and can be readily adapted for the sessions of a huge convention or the exhibits of a great exposition. The beautiful Music Hall seats 3,000. The Ball Room and Little Theatre have seating capacities of 1,500 and 700 respectively and ten other halls range in seating capacity from 90 to 500. A common stage makes it possible for the Main Auditorium and the Music Hall to seat 16,000 persons for a single event.

The Public Hall contains 260,000 square feet for exhibition purposes and every modern exhibit facility. The ceiling clearances are high. Unusual floor loads are sustained. Steam railway tracks solve one of the greatest problems of exhibitors.

The Hall is ideally located in the heart of the downtown district within easy walking distance of all principal hotels and shops—another assurance of good attendance at sessions or expositions.

The Public Hall is of fireproof construction and designed in Italian Renaissance architecture. The color and the diffused lighting in the main auditorium lend a warmth and softness unusual in buildings of such immense proportions. The Auditorium's acoustics have been declared perfect.

The Hall's $100,000 pipe organ is one of the finest in America. It has 10,010 pipes and 150 direct speaking stops. The echo organ is located in the rear of the Auditorium, 300 feet from the console.

Among other features of the building are spacious lobbies and corridors, wide ramps and stairways, committee rooms, lockers, telephone booths, women's and men's retiring rooms, emergency hospital, checkroom and telegraph stations. Nothing essential to the comfort of the patron has been overlooked in this colossal Public Hall.

The best testimonial as to the adequacy of Cleveland's convention facilities is the frequency with which the country's largest conventions and trade expositions return to this city. Many of the largest gatherings in the United States have met in Cleveland more frequently than in any other city.

*Recreation and Entertainment.* Cleveland offers a great variety of recreation. In summer there is the great park system, swimming in Lake Erie, golf, tennis, American League baseball, and numerous summer resorts. In winter there is dancing, ice skating, bowling, indoor golf and theatres.

Playhouse Square in Cleveland presents the highest grade of legitimate plays, vaudeville and sound productions. Twelve thousand seats are available in this theatrical district alone.

One of the most famous shopping streets in the world is Euclid Avenue with its array of fine shops. Their attractive and artistic window displays and their interior decorations are always of interest.

Cleveland's wide streets and broad sidewalks have been an important factor in its success as a shopping center. No large city in the United States is better equipped to handle large crowds of shoppers.

The shops themselves have wide aisles, easily accessible stairways, elevators and escalators—all of which facilitate shopping. The efficient arrangement of merchandise for which Cleveland stores are noted make the shopper's task easier.

To enable their clientele to secure the latest style originations, all of the larger Cleveland establishments maintain buyers in the foreign centers of fashion. Merchandise from every corner of the earth can be found in Cleveland.

Cleveland's many other attractions include beautiful residential sections, great universities and schools, interesting museums and historical points of interest.

Above all, visitors to Cleveland find a spirit of friendliness and they carry away pleasant memories and a desire to return.

### ENTERTAINMENT HEADQUARTERS

Few cities have so diversified amusements and entertainment of so high a character. There are hundreds of places to go, hundreds of things to do, hundreds of interesting things to see.

*Theaters and Dancing.* Cleveland's show houses present the cream of the nation's theatrical talent. In Playhouse Square, with its 12,000 seating capacity, theaters not only offer excellent productions, but they are also noted attractions in themselves. The spacious and

luxurious foyers contain art treasures valued at many thousands of dollars.

In the vicinity of Playhouse Square and scattered throughout the city are many excellent restaurants offering entertainment and dancing. Two of the largest and most elaborate public ballrooms in the world are found in Cleveland.

If you seek the outdoors, there is, in summer, American League Baseball; Euclid Beach Amusement Park, Edgewater and Gordon Parks give opportunity for swimming, boating, and the like. There are also many interesting boat excursions or outings to one of the many pleasure resorts dotting the shores of Lake Erie.

In fall and winter, Cleveland's recreation program is replete with football, basketball, hockey and other indoor and outdoor ice events, boxing bouts and other amusements. Three college teams and the many high school elevens offer a great football variety.

*Beautiful Parks.* Cleveland's park and boulevard system is unrivalled by any city in the United States in its picturesque natural beauty. Deep ravines, waterfalls, fine old forests, sandy stretches of beach, huge rock formations of Lake Erie's shoreline—all lend an unusual charm to the park system.

The Metropolitan Park System combines into one continuous outer encircling parkway the more important valleys and glens in Cuyahoga County and parts of the neighboring counties. Nine park reservations are included in the project which consists of approximately 90 miles of parkway and 15,000 acres of grounds. Two golf courses in Rocky River Valley are included in the system.

*Organized Sports.* Cleveland is a sport loving community. It was the birthplace of organized amateur baseball, as well as the National Baseball Federation, an organization with a membership of 30 cities which conducts annual intercity championship series. Seven hundred teams are represented in the association.

More than 30,000 registered athletes participate in organized sport in Cleveland every year, about one-third of whom play baseball. Industrial plants have about 60 baseball teams while 30 churches are represented.

There are many other sports in Cleveland.

Leagues operating under the Cleveland Basketball Commission have a total membership of more than 850 teams. Other organized sports include outdoor and indoor skating, ice baseball, outdoor and indoor swimming meets, soccer and football. One of Cleveland's Public swimming pools has a capacity of 5000 bathers.

## TRANSPORTATION TO THE CLEVELAND MEETING*

There will be no reduced rate for round trip railroad tickets, but the fare on all lines is now 2 cents a mile in coaches, and 3 cents a mile in Pullman cars, with extra fare for Pullman sleeper. All lines, except the Pennsylvania Railroad, come into the Terminal Station at the Public Square. The Pennsylvania Railroad has two stations, one at Euclid Avenue and East 55th Street, and the other, the old Union Station at West 9th Street. Passengers should go to the Union Station (end of the line) as that is within one mile of all down town hotels. The Cleveland Hotel (Headquarters) is in the Terminal Tower Building.

All Air Lines come in at the Cleveland Air Port which is about 15 miles from down town hotels. Taxi fare is 75 cents per person each way and is not included in the Airway ticket.

Members driving by automobile may leave their cars with the Doorman at all down town hotels or in the Garage in the Terminal Tower Building. The Garage charge is $1.00 for twenty-four hours, 75 cents for over night (6 P.M. to noon next day) or $5.00 for the week. This is "in and out" service as many times as you wish. There is no extra charge for "Doorman" service. Upon request to your Chairman, road and city maps, or any other information will be mailed directly to you before the meeting. When making hotel reservations, if members will signify how they are coming, we will forward the necessary information.

Members coming via Detroit will find overnight boat service on the D. and C. Line. The dock at the foot of E. 9th Street is within one mile of all down town hotels.

W. I. LeFevre, M.D., *Chairman*
*Transportation Committee*
9400 Euclid Avenue

* See also page 274.

## COMMERCIAL EXHIBIT

The Commercial Exhibit at the 1936 meeting of the American Roentgen Ray Society promises to be an unusually large and interesting one. Seventeen of the leading manufacturers have taken a total of forty-one spaces. The exhibit room is a large and attractive one next to the meeting hall with additional spaces in the large corridor outside of the meeting hall.

The following will give some indication of what those in attendance may see in the Commercial Exhibit:

At the Picker-Waite booth will be shown the complete Shockproof Therapy outfit, which incorporates many new safety devices. There will also be shown a compression serialograph which has been recently designed for multiple and rapid exposures of the duodenal cap.

Machlett Laboratories will exhibit their complete line of diagnostic and therapy tubes, including all of the latest developments in shockproof tubes for these purposes. Of special interest will be the revolutionary shockproof tube for intermediate x-ray therapy which they expect to show for the first time at this meeting.

Visitors to the Keleket Exhibit in Booths 20, 21, 22, 23, 24 and 25 will have an opportunity to view one of the greatest advances made in recent years in the design of oil immersed shockproof deep therapy x-ray equipment. The new Keleket self-contained oil immersed shockproof 200 kv. deep therapy x-ray apparatus will be on display. This unit ideally meets the requirements of the experienced roentgenologist providing the maximum of conveniences in positioning the deep therapy x-ray tube in treatment work. Then, too, there will be on display a complete self-contained x-ray unit which offers facilities for fluoroscopy, roentgenography and Potter-Bucky diaphragm roentgenography. This complete outfit features the latest shockproof design and occupies a limited floor space so as to provide for practically any installation difficulty. The exhibit will contain other new developments as well as a large and attractive display of roentgenograms.

The Philips Metalix Corporation will exhibit the following: a new shockproof shield with cables of small dimensions and light weight; double focus heavy anode tubes, 2/6 and 2/10 kw.; shockproof and non-shockproof Rotalix tubes; improved Kromiron and Metalix tubes of small overall dimensions; Metalix valves; new 10 ma. shockproof therapy tube with grid for use on Villard circuits, having the same emission as constant potential.

The exhibit in the booths of the Eastman Kodak Company will consist of a collection of interesting roentgenograms including a series of the entire spine made in one exposure using 14″×36″ film. In addition, there will be displayed a number of interesting photographs demonstrating infrared photography in clinical practice, together with a display of clinical photographic transparencies made with Translite Film. Technical representatives will be in attendance and they will be glad to discuss any problems in connection with roentgen-ray or clinical photographic procedures. A complete line of Cine-Kodak equipment will also be on display for those interested.

The Standard X-Ray Company plan on exhibiting their shockproof rayproof deep therapy tube stand complete with generator, oil cooling system, and filter indicator. Their set-up will be such that they can demonstrate the safety features of both the oil cooler and the filter indicating device. These should be of interest to anyone using deep therapy equipment. They will also exhibit x-ray generators of other capacities.

The Patterson Screen Company will demonstrate only fluoroscopic and intensifying screens. Mr. Patterson and Mr. Reuter will attend the meeting and will be very glad to discuss screen problems.

The Fink-Roselieve Company, Inc., manufacturers of photographic chemicals, will display their products, the Concentrated Liquid X-Ray Developing and Fix-

ing Solutions. Beyond familiarity with the ease of preparation, knowledge of the exceptional working qualities of these solutions will prove of great interest to the roentgenologist, full details of which can be obtained from the representative in the booth.

The exhibit of the Gevaert Company of American will consist of the showing of roentgenograms made under interesting conditions of technique with Gevaert x-ray film. It will also comprise a demonstration of clinical photography, showing the interesting results that can be secured through proper choice of sensitized material. There will also be a demonstration of Concentrated Liquid Processing Solutions.

In the booth of the Agfa Ansco Corporation three x-ray films made by them will be exhibited. The regular Agfa X-Ray Film will be shown on an improved base. This base is adapted for more pleasing and effective showing either under mercury vapor or incandescent illumination. Also will be exhibited Agfa X-Ray Film for non-screen technique. This new medium has proved unusually popular, and is becoming widely accepted where bone and soft tissue detail is essential. The third product to be exhibited will be Agfa Direct Duplicating Film, which handled like ordinary contact printing paper, gives a duplicate negative of any roentgenogram from which copies are desired. It is possibly most generally used in copying portions of negatives containing the points of pathological interest. This is a new product, as it has never before been possible to obtain photographically a negative from a negative without an intermediate step.

In addition to the above the following will have interesting exhibits: DuPont Film Manufacturing Corporation, Buck X-Ograph Company, General Electric X-Ray Corporation, Victoreen Instrument Co., Westinghouse X-Ray Co., Adlanco X-Ray Corporation and Davies, Rose and Company.

## CANCER INSTITUTE*

### SEPTEMBER 7 TO 9, 1936

*Conducted by Medical School, University of Wisconsin, Madison*

### MONDAY FORENOON, SEPTEMBER 7

SERVICE MEMORIAL INSTITUTE

Room 230

9:15 Address to Visitors, Faculty and Medical Students. Glenn Frank, President, University of Wisconsin, Madison, Wisconsin.

CANCER AND INHERITANCE

9:30 The Influence of Extrinsic Factors in the Development of Induced Tumors in Animals. Dr. Leiv Kreyberg, University of Oslo, Oslo, Norway.

10:15 The Influence of Intrinsic Factors in the Development of Tumors in Mice. Dr. C. C. Little, Director, Roscoe B. Jackson Laboratory for Cancer Research, Bar Harbor, Maine.

11:00 Familial Occurrence of Cancer. Dr. Madge Thurlow Macklin, Associate Professor of Histology and Embryology, University of Western Ontario, London, Ontario.

### MONDAY AFTERNOON, SEPTEMBER 7

SERVICE MEMORIAL INSTITUTE

Room 230

CANCER AND INHERITANCE

2:00 Hormones and the Development of Atypical Growths and Malignant Tumors. Dr. Edgar Allen, Professor of Anatomy and Chairman of Department, Yale University Medical School, New Haven, Connecticut.

2:45 Carcinogenic Substances in the Production of Tumors in Laboratory Animals. Dr. H. B. Andervont, Biologist, U. S. Public Health Service, Boston, Massachusetts.

ROUND TABLES

SERVICE MEMORIAL INSTITUTE

Room 230

3:45 Diagnostic Problems in the Recognition of Early Cancer. Dr. S. P. Reimann, Leader, Pathologist and Director of the Research Institute of the Lankenau Hospital, Professor of Experimental Pathology in the Graduate School of the University of Pennsylvania, Philadelphia, Pa.; Dr. Emil Novak, Associate Gynecologist, Johns Hopkins Medical School, Baltimore, Maryland; Professor Henry Cou-

* The Wisconsin Alumni Research Foundation has made available the necessary funds to finance this Institute.

tard, Chief of the Department of X-Ray Therapy for Cancer, Radium Institute of the University of Paris, Foundation of Curie, Paris, France.

SERVICE MEMORIAL INSTITUTE

Room 506

Genetics—Inheritance and Cancer. Dr. Leiv Kreyberg, University of Oslo, Oslo, Norway; Dr. C. C. Little, Director, Roscoe B. Jackson Laboratory, Bar Harbor, Maine; Dr. Madge Thurlow Macklin, Associate Professor of Histology and Embryology, University of Western Ontario, London, Ontario.

SERVICE MEMORIAL INSTITUTE

Room 301

Filterable Viruses and Cancer. Dr. J. B. Murphy, Leader, Director of Cancer Research, Rockefeller Institute for Medical Research, New York City; Professor B. M. Duggar, Professor of Physiological and Applied Botany, University of Wisconsin, Madison, Wisconsin.

## MONDAY EVENING, SEPTEMBER 7

SERVICE MEMORIAL INSTITUTE

Room 230

Broadcast 8:00 P.M. to 9:00 P.M. over WIBA Madison—1280 Kilocycles

8:00 Cancer, a Public Health Problem. Dr. James Ewing, Professor of Oncology, Cornell University Medical College, Memorial Hospital for the Treatment of Cancer, New York City.

## TUESDAY FORENOON, SEPTEMBER 8

SERVICE MEMORIAL INSTITUTE

Room 230

9:00 The Influence of Wave Length on the Biological Action of Radiation. Dr. Gioacchino Failla, Physicist, Cancer Memorial Hospital, New York City.

10:00 The Reaction of Tissue Cells to Irradiation. Professor Henry Coutard, Chief of the Department of X-Ray Therapy for Cancer, Radium Institute of the University of Paris, Foundation of Curie, Paris, France.

11:00 Tissue Culture in the Study of Cancer. Dr. Warren H. Lewis, Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland.

## TUESDAY AFTERNOON, SEPTEMBER 8

SERVICE MEMORIAL INSTITUTE

Room 230

2:00 The Biology of the Cancer Cell. Dr. S. P. Reimann, Pathologist and Director of the Research Institute, of the Lankenau Hospital, Professor of Experimental Pathology in the Graduate School of the University of Pennsylvania, Philadelphia, Pa.

2:45 Filterable Viruses in Malignant Neoplasms. Dr. J. B. Murphy, Director of Cancer Research, Rockefeller Institute for Medical Research, New York City.

ROUND TABLES

SERVICE MEMORIAL INSTITUTE

Room 230

3:45 Surgery and Irradiation in the Treatment of Cancer. Professor Henry Coutard, Leader, Chief of the Department of X-Ray Therapy for Cancer, Radium Institute of the University of Paris, Foundation of Curie, Paris, France; Dr. Gioacchino Failla, Physicist in Charge of Radiology, Cancer Memorial Hospital, New York City; Dr. Emil Novak, Johns Hopkins Medical School, Baltimore, Maryland.

SERVICE MEMORIAL INSTITUTE

Room 506

Cytology of Malignant Neoplasms. Dr. James Ewing, Leader, Professor of Oncology, Cornell University Medical College, Memorial Hospital for the Treatment of Cancer, New York City; Dr. S. P. Reimann, Pathologist and Director of the Research Institute of the Lankenau Hospital, Professor of Experimental Pathology in the Graduate School of the University of Pennsylvania, Philadelphia, Pa.; Dr. Warren H. Lewis, Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland.

SERVICE MEMORIAL INSTITUTE

Room 301

Etiology of Cancer. Dr. H. B. Andervont, Leader, Biologist, U. S. Public Health Service, Boston, Massachusetts; Dr. J. B. Murphy, Director of Cancer Research, Rockefeller Institute for Medical Research, New York City; Dr. Edgar Allen, Professor of Anatomy and Chairman of Department, Yale University Medical School, New Haven, Connecticut.

## TUESDAY EVENING, SEPTEMBER 8

*Open to the Public*

GREAT HALL, MEMORIAL UNION

Broadcast 8:00 P.M. to 9:00 P.M. over WIBA Madison—1280 Kilocycles

8:00 A Program for the Control and Prevention of Cancer. Dr. C. C. Little, American Society for the Control of Cancer, New York City.

## WEDNESDAY FORENOON, SEPTEMBER 9

*Joint Meeting with the State Medical Society of Wisconsin*

GREAT HALL, MEMORIAL UNION

9:00 Biopsy in the Recognition and Treatment of Early Malignancy. Dr. James Ewing, Professor of Oncology, Cornell University Medical College, Memorial Hospital for the Treatment of Cancer, New York City.

9:40 The Relation of Filterable Viruses to Malignant Neoplasms. Dr. J. B. Murphy, Director of Cancer Research, Rockefeller Institute for Medical Research, New York City.

*Twenty Minute Intermission*

10:40 The Effect of Bacterial Products on the Growth of Malignant Tumors. Dr. H. B. Andervont, Biologist, U. S. Public Health Service, Boston, Massachusetts.

11:30 The Recognition and Treatment of Early Malignant Lesions of the Uterine Cervix. Dr. Emil Novak, Associate Gynecologist, Johns Hopkins Medical School, Baltimore, Maryland.

## WEDNESDAY AFTERNOON, SEPTEMBER 9

GREAT HALL, MEMORIAL UNION

2:00 Treatment of Cancer of the Breast. Professor Henry Coutard, Chief of the Department of X-Ray Therapy for Cancer, Radium Institute of the University of Paris, Foundation of Curie, Paris, France.

2:40 The Genetic and Constitutional Aspects of Spontaneous and Induced Tumors. Dr. Leiv Kreyberg, University of Oslo, Oslo, Norway.

*Twenty Minute Intermission*

3:40 Glandular Dysfunction and the Development of Malignant Tumors. Dr. Edgar Allen, Professor of Anatomy and Chairman of Department, Yale University, New Haven, Connecticut.

4:20 A Study of the Occurrence of Cancer in Different Individuals of the Same Family. Dr. Madge Thurlow Macklin, Associate Professor of Histology and Embryology, University of Western Ontario, London, Ontario.

## AIRPLANE SERVICE TO CLEVELAND

Airplane passenger service from all parts of the United States to Cleveland is available for those who desire to utilize this speedy form of transportation to attend the American Roentgen Ray Society and the American Board of Radiology. There is practically no city in the United States more distant from Cleveland than sixteen and one-quarter hours by airplane and there is overnight service from points as distant as 2,000 miles. Frequently a combination of rail-plane service offers speedy travel for those living in cities not directly on air lines.

Illustrative of travel time by multi-motored planes from various points to Cleveland are the following examples, the figures indicating approximate hours of travel from those points to Cleveland:

From Chicago, one hour and forty-eight minutes; from New York, two hours, fifty minutes; from Philadelphia, two hours and a half; from Detroit, fifty minutes; from Omaha, four and one-half hours; from Milwaukee, two hours and forty-five minutes; from Minneapolis, five hours; from Denver, eight and three-quarter hours; from Los Angeles and San Francisco, fourteen and one-quarter hours; from Portland, fifteen hours; from Seattle, sixteen and one-quarter hours.

Detailed information on any air or air-rail trip from any part of the United States to Cleveland will be gladly furnished by any United Air Lines' ticket office, or from any other air line ticket office, Postal or Western Union offices or travel bureaus.

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# ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

## ROENTGEN DIAGNOSIS

### HEAD

Erdly, J. Die Röntgendiagnostik der Hypophysengeschwülste. (The roentgen diagnosis of pituitary tumors.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1935, *51*, 125.

The author discusses the changes in the sella and surrounding regions caused by intrasellar, suprasellar, infrasellar, parasellar, retrosellar and presellar tumors, and in addition the changes that accompany hydrocephalus. He differentiates acromegalic from nonacromegalic pituitary tumors. He discusses in detail the differences in destruction of the sella in cases of supra- and retrosellar tumors which are caused by internal hydrocephalus and which are in general due to increased pressure of extrasellar origin. In these cases changes in the sphenoid sinus may help in differential diagnosis. Deformity or displacement of the third ventricle caused by destruction of the sella may appear in the ventriculogram. If the hydrocephalic ventricle impinges on the sinus it gives a sharply outlined, regularly arched shadow which is homogeneous and convex below. The multiplicity of contours of the floor of the sella is next taken up and the author shows that a dilated hydrocephalic ventricle can produce several contours of the sella. A differential point is that the multiple contours caused by herniation of the ventricle are usually concentric to each other whereas those caused by tumor are irregular.—*E. T. Leddy.*

Schüller, A. Haematoma durae matris ossificans. (Ossifying hematoma of the dura.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1935, *51*, 119.

Schüller presents the findings in 4 patients who had ossifying hematoma of the dura and adds 2 post-mortem specimens.—*E. T. Leddy.*

Dyes, O. Verkalkte Hirnrinde. (Calcified cerebral cortex.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1935, *51*, 409.

In the American and English literature there is not uncommonly described a syndrome of epileptic attacks, facial vascular tumors and linear calcifications over one of the cerebral lobes, usually the occipital. It has been shown that these striations are due to cortical calcification. In addition to these striations there may be also fine calcified spicules in the affected lobes.—*E. T. Leddy.*

Peiper, H. Über die ventrikulographische Voraussage des Charakters von Hirngeschwülsten. (The prediction of the character of a brain tumor from the ventriculogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1935, *51*, 113.

The author feels that a ventriculogram combined with the neurologic findings generally does not permit diagnosis of the type of brain tumor present. The ventriculogram does not permit differentiation of benign from malignant gliomas and meningiomas although serial ventriculograms may help. A negative ventriculogram does not exclude the presence of a brain tumor.—*E. T. Leddy.*

Schlesinger, B. Zur Technik und diagnostischen Auswertung des Enzephalo- und Ventrikulogramms. (The technique and diagnostic evaluation of encephalograms and ventriculograms.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1935, *51*, 221.

Schlesinger reports a group of 52 patients who had ventriculography or encephalography carried out as a diagnostic procedure and in 28 of whom a diagnosis of brain tumor was made. In 26 of these patients the diagnosis was made correctly and the author discusses these 52 cases in detail. He points out how it is necessary to correlate the roentgenologic, clinical and neurologic findings, and assigns greatest importance to the former.—*E. T. Leddy.*

Pounders, Carroll M. Congenital osteosclerosis (marble bone). *Ann. Int. Med.*, Feb., 1935, *8*, 966–971.

Though several theories as to the etiology of osteosclerosis have been suggested, the author is led to believe that "it is a hereditary, familial and constitutional disease of unknown etiology which may begin in utero." The essential pathology is a proliferation of fibrous tissue

and endosteal bone with resultant crowding and even obliteration of the marrow cavity. Roentgenography may reveal numerous transverse striations or perhaps evidence of old fractures. The most frequent sites of involvement include the upper ends of the humeri, the lower ends of the femora and the short long bones. The skull may show condensations and enlargements particularly of the posterior clinoid processes. Necrotic lesions of the alveolar border of the lower jaw are not uncommon. The patient is usually slender and frail, presenting the appearance of having a hydrocephalus with mental retardation. Dentition is usually delayed and early loss of the teeth because of caries is common. Several of the reported cases died as the result of suppuration and necrosis of the lower jar. Elsewhere, fractures are incurred with minimal trauma and healing is usually delayed. There may be a marked anemia or even a leukemic reaction, with enlargements of the liver and spleen (probably because of hematopoietic activities by these organs). Optic atrophy even to extreme blindness may occur in the late stages. Cure of the condition seems to be hopeless. The author recommends iron but believes that calcium, phosphorus, cod-liver oil, ergosterol and other substances which might promote the growth of bone should be avoided.

A case report of a 3½ year old boy is presented. His condition had been considered due to rickets and syphilis; the skeletal findings were accidental. He had been brought in for study because of blindness, enlargement of the head and inability to walk. Included in his past record was mention of a difficult delivery due to a dry labor and feeding problems until the age of five months when he was weaned. Cod-liver oil and orange juice were started at three months. Splenic enlargement had been noted even at that time and as early as six months it had been noted that the child's eyesight was not good. Though he sat up at about the age of six months, and crawled soon after that, he was never able to walk. He talked early and seemed alert mentally. At the age of 3½ he weighed only 28.5 pounds. He appeared hydrocephalic and presented many conspicuous deformities. He was almost totally blind. He had only four teeth and the liver and spleen were markedly enlarged and very hard. His hemoglobin was 60 per cent; total red blood cells, 2,600,000, showing marked anisocytosis; white blood cells up to 14,000, with a polymorphonuclear percentage of only 38. The blood calcium was 14.4 mg. and the inorganic phosphorus 5.4 mg. per 100 c.c. The spinal fluid pressure was increased. During the course of study and treatment he developed purpuric spots over his body. He died as the result of a fall—probably because of intracranial hemorrhage.—*A. A. de Lorimier.*

McGregor, Leone. A report of eleven instances of adamantinoma with a review of the malignant cases in the literature. *Acta radiol.*, 1935, *16*, 254–274.

The author describes 11 cases of adamantinoma of the jaw treated at the Radiumhemmet, Stockholm, and reviews the 28 atypical and more or less malignant cases described in the literature, with the object of determining whether there are any histological features that indicate that a tumor is malignant and apt to metastasize. The article is profusely illustrated with photomicrographs. There were some such atypical microscopic findings including: (1) a great richness of the stroma in cells which in some cases was as great as in fibrosarcoma; (2) a predominance of cuboid epithelium over the stellate or cylindrical types, and (3) a preponderance of epithelium over stroma with intricate arborization of the epithelial processes.—*Audrey G. Morgan.*

### NECK AND CHEST

Mattick, W. L., and Thibaudeau, A. A. Extramedullary plasma-cell tumors of the upper air passages. *Am. J. Cancer*, March, 1935, *23*, 513–521.

Extramedullary plasma cell tumors have been considered, by some authorities, to be of neoplastic nature; by others, as inflammatory, and by some, as a granulomatous reaction to specific toxic agents. Therefore the nomenclature has varied. Such terms have been applied as "granuloma plasmacellulare," "plasmocytoma," "plasma sarcoma," etc. The case being reported, the authors believe, is definitely neoplastic. Histologically, it resembled a true plasma cell myeloma.

The patient was a sixty-one year old male. His complaint was difficulty in breathing,which symptom had been developing over a period of two or three years, with progressive severity. Two small sessile tumors were found; one behind the soft palate, in the nasopharynx; the other in the hypopharynx just above the larynx The blood Wassermann and Kahn reactions

were positive (++). The tumors were excised, cutting with a snare and applying diathermy to the base. Histologically, they showed a dense growth of plasma cells, these for the most part being encapsulated by a fibrous stroma. In places the stroma and even the squamous mucous membrane overlying had been invaded. The central portions showed many blood and lymph channels. About these there appeared to be a tendency toward shoot-like arrangement of the plasma cells. Many of the capillary channels showed distention with a mucoid substance. In places, this substance seemed to have caused the endothelium to disintegrate. Round cells were absent except where tumor cells had infiltrated the fibrous and mucous cells.

This patient was seen at intervals up to three months after the excisions. No recurrences could be found. The authors are watching the urine for Bence-Jones protein and the skeleton for roentgenographic evidence of myeloma. In case of any signs of recurrence they plan to proceed with radiation therapy. They count this as the twentieth case of this type of tumor involving the upper respiratory passages.—*A. A. de Lorimier.*

Steiner, Paul E., and Francis, Byron F. Primary apical lung carcinoma. *Am. J. Cancer*, Dec., 1934, *22*, 776–785.

Complete case reports are given of 3 cases of carcinomas occurring at the apex of the lung; 2 studied at autopsy, 1 by biopsy. Two cases are of the type described by Pancoast and presented Horner's syndrome without roentgenological evidence of bone destruction in the upper three ribs. While the histopathological appearance might well indicate a pulmonic origin, there was no evidence that they arose in bronchial pouch remnants. There was no change in size of the tumors during the period of observation. In 2 of the cases, tonsillectomies had been performed, presumably because the shoulder pain was thought to be of rheumatoid origin.—*W. R. Brooksher.*

Kjellberg, Sven Roland. Zur Röntgendiagnose von Fremdkörpern im oesophagus mit besonderer Berücksichtigung von Spreizsymptomen und ortlicher Anschwellung der Oesophaguswand. (Roentgen diagnosis of foreign bodies in the esophagus with special reference to dilatation and local swelling of the wall of the esophagus.) *Acta radiol.*, 1935, *16*, 478–484.

With the methods now available foreign bodies in the esophagus can be diagnosed indirectly even when they do not give very much contrast. If there is a suspicion of foreign body a systematic examination must be made of the hypopharynx and esophagus. If the body is large the passage of food is obstructed. If it is small contrast medium will be retained above and around it. A clear spot the size of the foreign body can be seen in the shadow. If the mucous membrane is injured small air bubbles may penetrate the wall of the esophagus. Similar air bubbles may be produced by air-forming bacteria, however, and do not necessarily show the presence of a foreign body. There is local swelling of the soft tissues around the foreign body and the esophagus is dilated and the mucous membrane folds pushed apart. Six illustrative cases are described.—*Audrey G. Morgan.*

Jansson, Gösta. Die Röntgendiagnose bie intrathorakalem Neurinom. (Roentgen diagnosis of intrathoracic neurinoma.) *Acta radiol.*, 1935, *16*, 411–419.

Neurogenic tumors originating from the nerve roots in the spinal canal, or neurinomas, often assume the form of so-called hour-glass tumors with an intraspinal and a paravertebral portion. The author describes such a tumor in the region of the 6th to 8th thoracic vertebrae in a woman of forty-four. The intrathoracic portion of the tumor produced a characteristic shadow in the posterior mediastinum paravertebrally to the left of the spinal column. The few similar cases that have previously been published are reviewed.—*Audrey G. Morgan.*

Chaoul, H. Über die Tomographie und insbesondere ihre Anwendung in der Lungendiagnostik. (Tomography with special reference to its value in pulmonary diagnosis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1935, *51*, 342.

Chaoul points out the value of the tomograph in making roentgenograms of the various levels of the body, and in this paper he pays particular attention to the study of the lungs by this apparatus. He presents roentgenograms to show the superiority of this method over all others including stereoscopy—in demonstrating the pulmonary vessels, the normal and pathologic bronchi, consolidations and cavities in the lungs. The apparatus is simple to use and the time of exposure is short.—*E. T. Leddy.*

Lins, Aguinaldo. Constituição e diagnostico radiologico. (Constitution and roentgen diagnosis.) *J. dos clin.*, Nos. 8 and 9, 1934.

The constitution of the individual has a great deal to do with the position and relationship of the organs as seen in the roentgenogram. There are two chief types, the short and broad or brevilinear, and the long and slender or longilinear. The normotype is the mean between these extremes that appeals most to the esthetic sense.

The author describes and illustrates the position of the abdominal organs in the brevilinear and longilinear types and discusses the differential diagnosis for aortic aneurysm from other intrathoracic conditions with which it may be confused, particularly mediastinal tumors, based on these constitutional factors. The outline of the aneurysmal sac spreads centrifugally from the mediastinum to the lateral walls of the thorax, its long axis following more or less the line that bisects the angle formed by the direction of the systolic impulse and the center of gravity. Roentgenograms are given showing the position and direction of aneurysm of the different parts of the aorta.—*Audrey G. Morgan.*

Scheidegger, S. Zur röntgenologischen Differentialdiagnose der Miliartuberkulose. (The roentgenologic differential diagnosis of miliary tuberculosis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1935, *51*, 209.

The author reports a case which was diagnosed miliary tuberculosis by roentgenologic examination. At autopsy the patient was found to have not tuberculosis but miliary bronchopneumonia.—*E. T. Leddy.*

Assmann, H. Die Darstellung des Frühinfiltrats im Röntgenbild. (The roentgenologic demonstration of early infiltration.) *Fortschr. a.d.Geb.d.Röntgenstrahlen*, Jan., 1935, *51*, *1*.

The author describes the roentgen appearance of early tuberculous infiltration of the lungs, and discusses their pathologic anatomy and differential diagnosis. He emphasizes that roentgen examination is superior to all other methods of investigation for making an early diagnosis especially of central lesions, which is extremely important for the patient who should have treatment as early as possible. Assmann points out that the entire clinical and roentgenologic pictures must be correlated.—*E. T. Leddy.*

Martin, D. Clifford, Pessar, Harry T., and Goldberg, Jacob A. A Tuberculosis survey among 2,000 food-handlers in New York City. *Am. Rev. Tuberc.*, 1934, *29*, 182–189.

The results of a survey of 2,000 apparently healthy food handlers is presented. At first the plan was to include in the examination: (1) the taking of a careful clinical history; (2) a thorough physical examination of the chest; (3) a roentgenogram of the chest; (4) the examination of the sputum; (5) an intracutaneous tuberculin test.

After examining the first 200 individuals, it became apparent that only the following were of value: (1) a routine roentgenogram of the chest; (2) an examination of the sputum; (3) a physical examination of the chest of those in whom a pulmonary lesion was demonstrated by the roentgen ray.

By this procedure active tuberculous pulmonary lesions to the extent of approximately 2 per cent were found in apparently healthy food handlers in New York City. The authors believe this represents the average situation in all large urban communities. This percentage represents the existence of not less than 6,500 cases of unknown and therefore uncontrolled active pulmonary tuberculosis in New York City. In addition, there was evidence of many thousands of cases of arrested tuberculosis, latent childhood tuberculosis and pleurisy among these food handlers.

A good chest roentgenogram was found to be the most effective means for the successful demonstration of the existence of tuberculous pulmonary lesions. The authors believe that when the question of tuberculosis is involved, no physical examination of the chest is worth its name without the roentgenogram.—*L. H. Osmond.*

Watts, H. F. R. Childhood-type tuberculosis, as revealed by the x-ray. *Am. Rev. Tuberc.*, 1934, *29*, 424–429.

Of the 10,639 patients in this series studied in the clinics of the Boston Health Department, 7.5 per cent of the adult group (seventeen years of age or more) showed evidence of childhood type tuberculosis, uncomplicated by phthisis; 22.5 per cent showed evidence of phthisis, without evidence of the childhood type; while 2+ per cent had both types of the disease. The group of children showed 9 per cent with childhood type lesions unaccom-

panied by adult phthisis, 0.3 per cent with adult phthisis, unaccompanied by the childhood type, while 0.2 per cent had both types.

The presence of areas of calcification, whether they be within the lymph nodes or occur as isolated, minute areas within the lung parenchyma, where they represent a calcified primary lesion, is accepted as evidence of the childhood type of tuberculosis. All fibrosing parenchymal lung areas in the child are regarded as belonging to the childhood type group. All pneumonic shadows in the child are regarded as potential tuberculous pneumonias.

The author is impressed with the large number of children having childhood type lesions who have been watched for a long period of years without developing the adult type of disease; with finding the adult type alone more often than the adult type superimposed upon the childhood type; and with the large number of adults (7.5 per cent) showing childhood type lesions without adult type lesions as contrasted to the 22.5 per cent with manifest adult type tuberculosis in whom characteristic lesions of the childhood type were not in evidence. Of 92 adults having evidence of both childhood and adult types, it has been noticeable that the superimposed adult lesions were frequently moderate or minimal in extent.—*L. H. Osmond.*

Wallgren, Arvid. Primary pulmonary tuberculosis in childhood. *Am. J. Dis. Child.*, May, 1935, *49*, 1105–1136.

It is now generally accepted that tuberculous infection occurs, as a rule, through the inhalation of tubercle bacilli. The result is a pneumonic inflammatory process but histologically the pneumonia does not have the appearance that is characteristic of tuberculosis. It may affect only a few alveoli or in serious cases it may gradually involve the greater part of an entire lobe. It can only be recognized by the presence of a great number of tubercle bacilli. This tuberculous pneumonia is called the primary focus; it is the first anatomic lesion in the organism produced by the infection. Soon after the lungs have been infected the tubercle bacilli spread from the alveoli along the lymphatics to the regional glands in the hilus. The primary focus, the tuberculous lymphangitis and the glandular lesions are called the primary complex.

Forces mobilized under the influence of the infection are of two kinds: the one consists of phenomena that make the child less susceptible to new exogenous infections and enable it to restrict the infection in progress; the other, of phenomena that cause the organism to react more intensely to the bacilli and their toxins. The first type corresponds to immunity; the second to hypersensitivity or allergy in a narrow sense.

Clinically the first lesion is not demonstrable, namely, the formation of a wall of lymphocytes which forms about the primary focus, while an area of caseous necrosis develops in the center of the lesion. The only possibility of verifying the lesion clinically is by the recovery of the tubercle bacilli in the gastric lavage contents. In several cases, this was found a week before sensitivity to the tuberculin reaction occurred. The period of incubation varies from three to seven weeks. The end of the period of incubation is marked by the appearance of allergy indicated by enlargement of the lymphatic glands and often by an extensive pulmonary lesion, in the center of which a caseous focus may be found. The pathognomonic symptom indicating this stage is the positive sensitivity of the child to tuberculin. Another sign that usually very soon develops is fever, which is subject to wide variation and which has a comparatively short duration as the only typical characteristic. This is entirely different from the febrile or subfebrile temperature of long duration that is usually associated with tuberculosis. If the initial high fever continues a long time it is highly probable that malignant tuberculosis is developing. When sensitiveness develops to tuberculin and the allergy is high, a child often reacts with symptoms of illness due to a previously latent nonspecific infection.

Wallgren believes that erythema nodosum stands in intimate connection with tuberculosis. It arises just at the time the organism has become sensitive to tuberculin. If erythema nodosum occurs, a child should be regarded as infected with tuberculosis, at least until a negative reaction to tuberculin has proved the contrary.

He states that primary tuberculosis may appear in three ways: (1) with a positive reaction to tuberculin only; (2) with a positive reaction and fever; (3) with a positive reaction, fever and erythema nodosum. In the last two groups a marked perifocal allergic reaction arises around the tuberculous foci.

As a rule, physical examination yields only negative results in primary tuberculosis and one is amazed, Wallgren states, to find such definite roentgen changes in these cases and illustrates this fact by the roentgenograms which are reproduced. There is nothing pathognomonic in the roentgenogram of fresh primary tuberculosis. Thus a reliable diagnosis is not possible by means of the roentgenogram alone. But if the symptoms point to the disease, the physician can, with its help, discover whether the process is localized intrathoracically and in such cases, the extent of the lesion. Symptoms found are a typical expiratory stridor and a peculiar cough called by Wallgren bitonal. This consists of two notes, a lower one corresponding to the usual sound of coughing and a higher one that arises as the air, during the act of coughing passes through a narrowed passage such as might be caused by compression of a bronchus due to enlarged glands.

Primary pulmonary tuberculosis as a rule is benign. It is scarcely possible to predict whether it will follow its usual slow regression or whether it will become rapidly caseous and cavernous and with that pass over into the progressive primary tuberculosis. This second form may not necessarily lead to death. Progress may cease at any moment and the tuberculous tissue may heal. Healing takes place with sclerosis and calcification and with contraction of the involved part of the lung. Calcification as the final healing process is considerably commoner in children, especially in infants, than in adults. There are some infiltrations of tuberculous etiology which are of great extension and which recede entirely without caseation or contraction. The infiltration as roentgenologically seen consists then of noncaseous perifocal infiltration. However the probabilities of a malignant course are greater with a large infiltration than with a small one. High and protracted fever and the results of the sedimentation test point to caseous changes involving a considerable area.

In the main, the treatment of primary tuberculosis of the lung is the same for children as for adults: fresh air, rest, suitable diet and the avoidance of all injurious influences. It is true that this process often heals with no special treatment without the disease having been recognized in its initial stage, but it does not follow that a patient with fresh primary pulmonary involvement should not be treated. Rest is essential. How long a child should be kept in bed is debatable. Fever is one indicator for the extent of the bed treatment but a more refined index is the sedimentation test. Rest in bed should be maintained until this test is normal. In a case of more severe form, the sedimentation value remains high for months after fever has disappeared. Even under the most favorable conditions at home a neuropathic child should have hospital treatment. A change of environment has an exceedingly favorable effect. The general treatment also includes sunlight or artificial light. Wallgren does not begin this until a few months have elapsed after the onset of the disease and then continues it periodically during the winter months.

He does not use pneumothorax in these cases. No special medication as a rule is required; theoretically calcium therapy may be justifiable. Cod-liver oil in the usual doses seems to improve the general condition of ininfants during the winter; older children probably do not need it. The diet should be normal with a sufficient number of vitamins.

If in the roentgenographic examination of a child with a positive reaction to tuberculin, a calcified primary complex is found, the primary tuberculosis is generally regarded as unimportant so far as the health of the child is concerned. The tuberculosis is looked upon as clinically healed. However, it must not be lost sight of that this healing is healing in the clinical sense. Owing to the great resistance of the tubercle bacilli, they can remain alive and virulent in the calcified foci for many years. Not until death of these bacilli occurs can definite healing of primary pulmonary tuberculosis be claimed.

Wallgren's own clinical observations of the calcified primary complex support the notion that it may undergo considerable regressive changes, although he has not had an opportunity of observing a patient long enough to note complete disappearance. He has noted frequently roentgenographic regression. Many foci heal without roentgenographic calcified foci. Before the possibility of calcification is precluded several years must have elapsed, as it may take a long time in certain cases before calcification begins. This applies especially to infants.

The specific complications that arise subsequent to, and in direct connection with healed or healing primary pulmonary tuberculosis are reactivation with anatomic changes as occur in the onset of the process, and secondly,

in some cases, tertiary pulmonary tuberculosis. The nonspecific diseases that follow are bronchiectasis more closely related to the primary lung changes, and less closely related, meningitis, pleurisy, miliary tuberculosis and last, tertiary pulmonary tuberculosis.—*R. S. Bromer.*

Morgan, Roy. Certain aspects of pulmonary tuberculosis in children. *Am. Rev. Tuberc.*, 1934, *29*, 577–586.

From 1910 to 1932, 631 cases of pulmonary tuberculosis of the adult type in children and adolescents (under eighteen years of age) have been under observation. In the first group of 200 cases between 1910 and 1920, only 7 are known to be living. All had a positive sputum and 144 were classed as advanced on admission. The mortality has been very high in these cases in the remainder of the group, but results have been definitely better, especially in the minimal cases, since bed rest for at least one year for all cases was instituted in 1927. Artificial pneumothorax offers hopes of still further improving the results.

In the adult type of tuberculosis in children and adolescents, the logical procedure is to find the disease while it is early and curable. Clinics should be more widely conducted in the schools. —*L. H. Osmond.*

Smith, Charles Hendee. The tuberculosis of childhood. *Ann. Int. Med.*, March, 1935, *8*, 1090–1120.

The author scorns, when loosely applied, such terms as "masked juvenile tuberculosis," "occult tuberculosis," "active," "latent" or "hilus tuberculosis" and in many instances, the application of the terms "epituberculosis" or "miliary tuberculosis." He takes this stand because too oftentimes there is implied the idea that tuberculosis is an isolated disease involving only one organ. He believes that a more systemic involvement should be considered and that the sequence of pathology, from the site of primary invasion through the series of extensions, should be applied to each case. The primary focus can usually be found in the lung or the intestine but it may possibly be in the tonsil or any other "physiological surface of the body." Depending upon the number of organisms permitted to invade, from there, as conditioned by the resistance on the part of the patient, there may develop an inflammatory walling-off, or there may result an extension of the infection either directly to the regional tissues or indirectly after filtration into or through the regional lymphatics. With invasion of the blood vessels extensive dissemination takes place. By this means the return circulation may scatter the organisms to many areas of the lung but there the capillary filters are so inadequate that ultimate generalized miliary distribution usually takes place. Showers of blood stream dissemination may occur but if the number of organisms circulated each time be not too great the result will simply be localizations in such organs as the liver, the spleen, the bones or the kidneys. The patient might resist many or all of these deposits; such cases are not usually recognized as "miliary tuberculosis." Even though present in the lung, the primary focus may not be visualized roentgenographically until its activity is decreased by reaction fibrosis and calcification. The combination of the actual primary focus plus the drainage lymphatics is called the "primary complex"—the pathological evidence of which is so oftentimes spoken of as the "childhood type of tuberculosis." Regardless of fibrosis and calcification about these lesions, it is likely that complete healing is not effected. This fact is borne out by the observation that positive skin reactions, in these cases, can be expected throughout the life of the individual, whereas after Calmette inoculations of attenuated bacilli, "immunization" effects have been found to last only a few years. Massive involvement of regional lymphatics may produce bronchial obstructions with resultant atelectasis and fibrosis. Parenchymal spread about the primary lesion may result in "perifocal tuberculosis" which may progress to caseation and cavitation. Breakdown and spread by way of a bronchus results in "multiple focal lesions"—which should not be confused with "miliary tuberculosis." These lesions might be called "bronchogenic miliary" or "lobular tuberculosis"; they are much larger than true miliary lesions. With more massive invasion along the bronchial tree, there results a true "lobar tuberculosis." Some processes may appear to be lobar but really be an "epituberculosis." The latter cases clear up. They probably represent compression atelectasis or a "drowned lung" on the basis of mere exudation. Involvement of the larynx is relatively rare in children but tuberculous enteritis and secondary mesenteric adenitis are not uncommon developments due to coughing up and swallowing the bacilli.

The incidence of tuberculosis is highest among the poorer children in congested communities. Compiling the statistics as to skin tests, from several urban districts, it would appear that "about 10 per cent of living children give positive reactions in the first two years, 15 per cent in the third and fourth years, 20 per cent at five to seven, 30 per cent at seven to nine, and only about 40 per cent at ten to twelve." The total death rate does not reach 10 per cent for any age—therefore even during the first two years some of the cases of tuberculosis get well. However, the death rate is "high in the first two years, as high as any year until early adult life. It falls off rapidly up to five and the lowest rate is from five to 15, after which there is a steady rise." Many cases of transient unexplained fever with failure to gain weight or of so-called "marasmus" or "bronchopneumonia" should be skin tested for tuberculosis. Roentgenography may reveal large lesions in cases where no signs whatsoever can be elicited either before or after seeing the film, though in other cases of definite tuberculosis, both the physical and roentgenographic studies may be negative. Leukocytosis is to be expected in all acute or exudative forms.

In older children, skin testing and search for tuberculous foci should be prompted by such symptoms or signs as irregular fever—reaching 100 or more; failure to gain weight; langor; easy fatigability; anorexia; irritability; distressed facies; corneal phlyctenules; papulonecrotic dermatoses; spontaneous hydro- or pydropneumothorax; positive D'Espine, etc.

The usual dietary and supportive treatments are recommended. To compel recreational rest a good bed table which can fit across the lap of the patient is essential. Pneumothorax is not oftentimes applicable in the case of children.—*A. A. de Lorimier.*

Fales, Louis H., and Beaudet, E. A. The healing of tuberculous cavities. *Am. Rev. Tuberc.*, 1934, *30*, 225–237.

A second series consisting of 90 cases with pulmonary tuberculous cavitation treated with strict bed-rest (one year) is analyzed. The results of this analysis are very similar to those of the previous group which included 147 cases.

Cavities are classified as exudative, productive and fibrotic, as different types of cavities correspond quite uniformly to the pathological changes present.

It was demonstrated that the young or exudative cavities responded most favorably to strict bed-rest (66 per cent healed); the moderately old or productive cavities less favorably (43 per cent healed); and the old or fibrotic cavities unfavorably (only 17 per cent healed). The logical conclusions to be drawn are: (*a*) that young cavities should be treated quite differently from the older types; (*b*) that at the beginning all exudative cavities should be treated at once by strict bed-rest; that a large percentage of productive cavities should also be treated by strict bed-rest (continuance of rest depending on the results obtained), and the selection of the cavities for rest depending greatly upon the location of the cavity, its proximity to the pleura, the character of cavity walls, and the progression or retrogression of the lesion; but that practically all fibrotic cavities be recommended for surgical procedure at once.

In the treatment of tuberculous cavities by bed-rest, it is very necessary that patients be under frequent competent roentgenographic control, so that increase in size of the cavity or the development of new area of infiltration may be detected early, a warning to modify treatment, always having in mind surgical compression, to be resorted to when deemed expedient.—*L. H. Osmond.*

Overholt, Richard H. The roentgen-ray appearance of the lung fields in atelectatic bronchiectasis. *Am. Rev. Tuberc.*, 1935, *31*, 121–133.

Three cases of bronchiectasis of the left lower lobe are discussed in detail and emphasis is placed on the importance of the difference in the lung fields in the uninvolved portions of the lung and also the value of ascertaining the position of the posterior leaf of the diaphragm, as shown in the lateral roentgenogram.

In 2 of the cases, the relatively greater density of the right lung field as compared to the left at first lateralized the trouble in the right chest. Subsequent study in both cases demonstrated that the difference in lung density had been produced by a compensatory distention of the left upper lobe which was a response to the shrinkage of the left lower lobe. In both cases the shadow cast by the infected and shrunken lower lobe was obscured by the heart shadow. In both cases the shadow of the dome of the diaphragm on the involved side, as seen in the posteroanterior view, was in a normal position. Lateral roentgenograms

showed a marked elevation of the posterior leaf in each case. The third case, which was much more advanced, showed the secondary effects —evidence of compensatory emphysema in the left upper lobe and elevation of the left dome of the diaphragm—very clearly.

The secondary effects described above are quite important but one should remember that a greater radiability as seen throughout the left chest is often due to greater muscular development on the right. This appears to be playing a part in the first case presented as tissues not overlying the lung field are also more dense on the right than on the left. Therefore one must look for elevation of the posterior leaf of the diaphragm together with other evidence to make such a diagnosis roentgenographically.—*L. H. Osmond.*

Eloesser, Leo. Bronchial stenosis in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 1934, *30*, 123–180.

Stenosis of the air passages from the trachea to the bronchioles is not infrequently due to various tuberculous processes.

*Morbid Anatomy.* Tuberculosis may be responsible both directly and indirectly for stenosis of the bronchi. If we list stenoses according to the classification of v. Schrotter, the types of bronchial stenosis are as follows:

1. Intramural stenosis; ulcerating lymph node extruded into bronchial lumen.
2. Mural stenosis.
   a. Caseous ulcerative bronchitis.
   b. Submucous hyperplasia.
   c. Sclerotic shrinkage and distortion of bronchial wall.
3. Extramural stenosis.
   a. Extramural compression by enlarged peribronchial lymph nodes.
   b. Peribronchial sclerosis with extramural distortion and compression.
4. Diffuse stenosis of smaller air-passages (obliterative bronchiolitis).

*Pathology of Function.* Total obstruction of the trachea soon leads to death, but the tracheal caliber can be astonishingly reduced without killing the patient.

If the lumen of a lobar bronchus is totally obstructed, air is absorbed from the occluded lobe, the lobe collapses and finally carnifies and shrinks unless it contains purulent secretions, which when they are bottled up distal to an obstruction produce abscesses.

In intralobar stenosis (obstruction more distally than in lobar or main bronchus obstruction) atelectasis fails to follow, for, as Van Allen has shown, there are anastomoses between the distal air passages, so that air can pass into a blocked territory from an unblocked one (interalveolar communication).

In partial obstruction the distal lung is emphysematous and its volume increased.

Stenoses which intermittently open and close are most puzzling. Nontuberculous are perhaps more frequent than tuberculous ones. Physical signs and roentgenograms a few days apart will show sudden and remarkable change.

*Differential Diagnosis.* The diagnosis between fluid and stenosis is not difficult when the physiological changes are intelligently considered.

Much more difficult to differentiate from stenosis is the persistent diffuse fibrosis and atelectasis that one sees in lungs that have long been compressed by pneumothorax. Both give rise to clinical and roentgenographic appearances precisely similar. The reason for this similarity seems to be in the fact that both lead to the same result. Opaque oil will demonstrate a stenosis or its absence and so will the bronchoscope.

The signs of lobar stenosis are characteristic. The roentgen examination demonstrates the localized retraction, the narrow intercostal spaces, mediastinal and tracheal deviation, at times rise and impaired mobility of the diaphragm. The fact that there may be no atelectasis in an intralobar stenosis should be kept in mind as pointed out above.

Differentiation from a caseous lobar pneumonia should be easy in an aseptic stenosis; with the one patients are very sick, with the other not. However, with the stenotic retention of tuberculous pus differentiation is very difficult, the caseous consolidated lobe should retain its original size. The white count may help.

*Diffuse Obliterative Bronchiolitis.* One not infrequently encounters diffuse tuberculous emphysema. This has been described as tuberculous asthma and adduced to tuberculous allergy and to other causes equally mysterious. The emphysema has been seen in tuberculosis implanted upon or accompanying an old chalicosis. The emphysema is ascribed to a diffuse stenosing bronchiolitis, comparable to the fibrous bronchiolitis first described by Fränkel in patients subject to the fumes of destructive gases.—*L. H. Osmond.*

Bejlin, J. S. Lobulus accessorius inferior im Röntgenbild. (The roentgenographic appearance of lobulus accessorius inferior.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1935, *51*, 47.

The triangular shadow with a relatively sharp lateral border is often related to inflammation of the accessory lobe near the internal sinus. The affection is hard to diagnose and diagnosis is possible only by correlation of clinical and roentgenologic data. Roentgen examination is the method of choice for demonstrating the lesion. The signs described by Gräberger, Fleischner and others (position of the shadow, etc.) are not characteristic of this condition. The normal accessory lobe is often more easily recognizable than the pathologic. In the author's experience the lesion is more common on the left side.—*E. T. Leddy.*

Egbert, Dan S. Pulmonary asbestosis. *Am. Rev. Tuberc.*, 1935, *31*, 25–34.

The clinical and anatomical findings of a case of pulmonary asbestosis are presented, making a total of 28 cases with fatal terminations in the literature. In the apparently uncomplicated cases with fatal termination, it was determined that all were workers in asbestos factories; 9 of the 14 with age reported were between thirty-one and thirty-six years of age; the time of exposure to the dust before the onset of symptoms, when reported, averaged nine years, and the total time of exposure, when reported, averaged sixteen years. Active pulmonary tuberculosis was found to have been present in 6 instances of the 28 cases reported. In 3 instances death was primarily due to tuberculosis.

The morphological differentiation of asbestosis from other forms of pneumoconiosis rests upon the evidence of characteristic asbestosis bodies, and on the type and distribution of the pulmonary fibrosis; namely, it is diffuse, with a tendency to be more marked around the bronchioles. This is in distinct contrast to the well circumscribed, dense, hyalinized nodules of connective tissue seen in silicosis, in which condition the nodules form around and in the intrapulmonary lymphoid tissue, especially in the subpleural zone and in the tracheobronchial lymph nodes.—*L. H. Osmond.*

Reisner, Davis. The relations between extrapulmonary and pulmonary tuberculosis. *Am. Rev. Tuberc.*, 1934, *30*, 375–415.

The relations between extrapulmonary and pulmonary tuberculosis were studied on the basis of a series of 240 cases with clinically manifest extrapulmonary lesions which included the most frequent forms of extrapulmonary involvement. In nearly one-half, the lungs were either entirely free from changes or at the most presented evidence of an obsolete primary focus. Slightly more than one-half of the material showed evidence of postprimary pulmonary involvement. The differential analysis of the pulmonary changes from a morphological standpoint, based on careful roentgen-ray studies, revealed that approximately two-thirds (66.2 per cent) of the cases with positive findings exhibited as the most prominent features discrete nodular productive disseminations with a bilateral symmetrical distribution. As to the quantitative extent of these forms, various degrees of involvement were found; abortive types with sparsely scattered foci, numerous transitional forms of chronic disseminations of the miliary and acinonodose type with a more or less diffuse spread, and typical acute miliary disseminations. In one-third (33.8 per cent) of the cases with positive pulmonary findings, or in 17.5 per cent of the total material, no definitely characteristic morphological features could be found; this group presented the common forms of chronic pulmonary phthisis.

The extrapulmonary lesions represent in the majority of instances chronic generalized propagation of the infection, which leads to multiple organic manifestations, either with or without pulmonary involvement. The character of the chronic isolated organic phthisis (Ranke) was apparent in only about one-third of the total series. The predominance of the generalized forms was even more conspicuous in the cases in which the ultimate fate of the disease, that is, the condition at the time of death, could be studied. The pulmonary changes in extrapulmonary tuberculosis represent in the majority of cases a part of the chronic progressive endogenous generalization. The frequency of pulmonary involvement in these lesions is enhanced by the peculiarities of the pulmonary circulation and the rôle of the lung as a filter for circulating bacilli. From the standpoint of the mere frequency of the pulmonary changes, no definite antagonism could be noted as between extrapulmonary and pulmonary involvement. There is, however, a distinct antagonistic relation to the reinfection types

of pulmonary tuberculosis, especially to the active and progressive forms. The pulmonary tuberculosis at large presents a definitely more pronounced antagonistic relation to extrapulmonary involvement than vice versa; manifest extrapulmonary lesions are conspicuously rare in the common forms of pulmonary tuberculosis. The type of the chronic isolated phthisis is the general rule in pulmonary lesions, in contradistinction to the extrapulmonary forms. Acute miliary tuberculosis and meningitis present a comparatively frequent cause of death in chronic pulmonary lesions. This is consistent with the predominantly generalized character of extrapulmonary tuberculosis. Extensive and progressive pulmonary tuberculosis cannot be considered as a frequent cause of death in extrapulmonary lesions, if compared with the total proportion of coexisting pulmonary changes in these cases. This constitutes further evidence of the frequent benign and non-progressive character of the pulmonary involvement in extrapulmonary tuberculosis.

The frequency of pulmonary involvement is considerably lower in skeletal than in genitourinary lesions. The character of the chronic isolated extrapulmonary lesions is distinctly more manifest in the former than in the latter; it is most pronounced in the cases with tuberculous caries of the vertebrae. Various degrees of chronic hematogenous disseminations may occur in the lungs without clinically manifest extrapulmonary involvement.—*L. H. Osmond.*

Miller, James A. Haematogenous pulmonary tuberculosis. *Am. Rev. Tuberc.*, 1934, *29*, 489–520.

The evolution of the past and present concept of tuberculosis as a systemic infection is undertaken, pointing out the analogy of tuberculosis to the behavior of other bacterial diseases. In every bacterial infection one observes that generalization and localization coexist rather infrequently. Therefore, we must expect clinical forms of tuberculosis representing every form between overwhelmingly generalized and strictly localized disease. The bacteriological evidence of the systemic nature of tuberculous infection is not as constant as one should expect. However, considerable evidence is cited that bacillemia and hematogenous dissemination of tubercle bacilli certainly occur and probably occur in all forms of active tuberculosis.

Pathologically the pulmonary lesions of acute miliary tuberculosis are easily recognized by their even distribution, uniformity of size and histological features, being usually an exudative necrotizing process. In contrast, the lesions of chronic protracted hematogenous disseminated tuberculosis are characterized by uneven distribution, variations in size of lesions and variation in histological features from genuine miliary tubercles to nodular lesions of various size and conglomerate tubercles and caseous-nodose processes associated with marked fibrotic changes. These lung lesions are only one part of the general dissemination which is also characterized by caseous involvement of lymph nodes, exudates into serous cavities and lesions in other organs. Characteristic lesions of chronic hematogenous pulmonary tuberculosis are also represented by the exquisitely productive tubercles giving rise to fibrosis, the most frequent sites being in the upper lobe parenchyma and in peripheral subpleural and pleural areas. Another characteristic feature is the punched out cavity with its sharp, thin border embedded in normal or little-changed lung tissue and with the ability to enlarge or shrink with a rapidity little short of amazing and to disappear frequently leaving but a minimal trace. The amount of cough and expectoration is slight. The number of tubercle bacilli in the sputum are scanty. Frequently its most conspicuous feature is persistence for a long time without giving rise to bronchogenic spread and extension.

The practical importance of the conception of hematogenous pulmonary tuberculosis rests upon the possibility of recognizing its forms in practice. Acute miliary tuberculosis of the lung needs no description. The lesions of chronic protacted hematogenous dissemination occupy a position midway between acute miliary and the more localized forms. The more localized forms recognized as hematogenous disseminations have been termed by Bard as tuberculosis miliaris discreta, tuberculosis fibrosa densa and tuberculosis fibrosa diffusa, and can be picked out easily after a little study. Pleurisies with effusion are often probably of hematogenous origin. The punched out cavities are easily recognizable.

One of the outstanding characteristics of many of the clinical forms of hematogenous pulmonary tuberculosis is persistence of the lesions in some parts of the lungs without change over a period of many years. Even when symptoms such as hemoptysis, loss of nutrition, etc., are present, frequently the

lesions as demonstrated by the roentgenogram show there is a definite tendency to recurrence of lesions, which may be new hematogenous disseminations.

The author urges that one try to recognize lesions which are the result of hematogenous spread. In view of their relatively benign nature he thinks that we are wasting many months and years of active life and sanatorium and hospital beds needed for other cases.—*L. H. Osmond.*

Miller, James Alexander. Pulmonary tuberculosis as a part of a systemic infection (hematogenous pulmonary tuberculosis). *Ann. Int. Med.*, Sept., 1934, *8*, 243–257.

The conception that tuberculosis is a local disease of the lung, produced by the inhalation of tubercle bacilli, is too widely held by general practitioners of medicine. Hematogenous spread from either primary or secondary foci may be manifested in several forms; it is not restricted to that form which results when there is a massive dissemination of organisms to all parts of the body—with constitutional changes as seen in "general miliary tuberculosis." Blood stream invasion within a few hours after the first infection was demonstrated by Marmorek; Wilson's studies have suggested that "bacillemia occurs in about 5 per cent of all patients, and as a transitory phenomenon perhaps much more frequently." Considering the lungs in particular, reinfections might either be exogenous or endogenous—this latter avenue having early been considered by Aschoff, and, in recent years, gaining more and more consideration in a large percentage of cases.

The primary infection usually takes place in the lungs or intestine. Usually, the original lesion is slight and almost symptomless. There is early involvement of the regional lymphatics but with average tissue response the process is then halted. In the lungs this combination of the primary lesion plus the regional lymphadenopathy is called the "primary complex." This process quickly sets up a generalized reaction to the tuberculo-protein whereby resistance is developed against secondary infections. However, the primary infection may not be controlled in this manner; instead there may result a widespread extension, particularly in very young children, or repeated smaller disseminations of the organisms may cause multiple pulmonary lesions, perhaps with pleural involvement, or spread to the kidneys, skeleton, lymphatics or other organs of the body. Even minimal disseminations may produce marked constitutional reactions. In the lungs the secondary lesions, so developed, can be expected to be bilaterally distributed, particularly in the cortical areas of the upper lobes. If disseminations occur in crops, lesions of varying size will be found. From these secondary foci, organisms might break through the lung parenchyma into the bronchi, thereby producing pulmonary symptoms such as cough, expectoration, hemoptysis, etc. The condition might then be called "bronchopulmonary phthisis."

Some cases of bronchopulmonary phthisis are doubtless due to exogenous reinfection. Considering these, the author believes that "the upper lobe localization is characteristic, but they are apt, at first at least, to be unilateral and they are not apt to be associated with extrapulmonary lesions in organs not accessible to the outside." This form of tuberculosis shows less tendency to spread by way of the blood stream. However, bronchogenic spread is not an uncommon sequel. The secretions may carry the infection to other parts of the lungs or to the larynx or intestine.

Though recognition of the hematogenous origin is easy in acute generalized miliary or disseminated protracted progressive tuberculosis, decision as to exogenous development versus hematogenous spread is far more difficult or even impossible in cases of bronchopulmonary phthisis. Such evidence as recurrent deficiencies of nutrition, irregular fevers, digestive disturbances, undue malaise, fatigability, etc., point to the hematogenous background. The usual pulmonary symptoms are to be expected only after such lesions have opened into the air passages. If regional to the pleura, these lesions may produce an effusion—even in the absence of other pulmonary signs. Periodic roentgenographic studies may visualize disseminated lesions, showing either localized or radiating fibrosis, possibly calcification or even caseation and cavitation.

The author uses the recognized classifications but groups his cases into (*a*) the lymphohematogenous type with closed interstitial lesions or (*b*) the bronchopulmonary phthisis type, with extension through the air passages.

The usual therapeutic measures are mentioned: rest, ample nourishment, vitamins, heliotherapy, etc. In addition, the author believes that "even the rather generally dis-

credited tuberculin treatment still does appear in certain types of cases to have beneficial results." He cautions against the early use of collapse therapy in the hematogenous pulmonary cases, that is, "before they have gone over into the stage of bronchopulmonary phthisis."—*A. A. de Lorimier.*

Jönsson, Gunnar. Some roentgenological observations regarding pulmonary silicosis in porcelain workers. *Acta radiol.*, 1935, *16*, 431–438.

The main features of the roentgen picture in silicosis have been described but there are some details that have not been considered sufficiently. The author made roentgen examinations of 236 porcelain workers in a study of the question. He found that hilus changes have little if any value in the diagnosis of silicosis. They occur in many other pathological conditions and are absent in many cases of silicosis.

In Stage I of the disease there are small shadows the size of a pinhead or less; in Stage II larger shadows up to the size of a lentil or very small pea; in Stage III large massive shadows with contraction. It has been reported in the literature that the hilus shadows disappear in the third stage of the disease. The author holds that the shadows do not disappear but that they are distorted and displaced by contraction of the lung parenchyma to such an extent that they become hard to identify. The centers of contraction are in the posterior inferior portion of the upper lobe and the posterior superior portion of the lower lobe a couple of centimeters behind the hilus, corresponding to the area of distribution of two bronchi, the dorsolateral branch of the bronchus to the upper lobe and the first dorsal branch of the bronchus to the lower lobe.

The accumulation of dust in certain parts of the lung may be explained in two ways. It may be that more dust is inspired into these areas owing to varying pressure conditions in different parts of the lung or the dust may at first be uniformly distributed and afterwards removed from certain parts by coughing, etc.

As a result of the contraction in the last stage of silicosis, the trachea is drawn backward, sometimes to such an extent that it comes to lie almost immediately in front of the vertebral column. The main bronchi and vessels are drawn markedly to the side and, if the contraction in the upper lobe predominates, they are bent upwards.—*Audrey G. Morgan.*

Richter, H. Atemtechnik und Zwerchfellbewengung im röntgenographischen Bewegungsbild. (Respiratory and diaphragmatic movements as studied by the roentgen kymogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1935, *51*, 357.

The author here reports some observations made by the kymogram during various kinds of natural and artificially altered breathing and correlates the costal-diaphragmatic movements with changes in the kymograohic and spirometric readings.—*E. T. Leddy.*

Stanbury, W. Stuart. Anatomical changes in the diaphragm following phrenicectomy. *Am. Rev. Tuberc.*, 1934, *29*, 528–545.

The anatomical changes in the diaphragm following phrenicectomy as observed in 11 necropsies are reported. Only one case on human post-mortem material has been previously published, that in 1925 by Meisezahl. The duration of the paralysis noted in the series ranges from three weeks to six years. It was found that atrophy of the diaphragm is quite evident as early as the third week after section of the phrenic nerve and is complete by the fourth month. Histologically the atrophy of the paralyzed half of the diaphragm is seen to be complete and uniform. In one case only with four years' duration of paralysis a few normal muscle bundles were seen in one area. The author believes this probably represents an accessory nerve supply, rather than actual regeneration.

In view of the marked distortion of the abdominal viscera in 10 of the 11 cases, 3 of which had a fatal gastroduodenal obstruction, the possibility of such complications should be considered seriously when advising phrenicectomy for the treatment of pulmonary disease.—*L. H. Osmond.*

Schwatt, H. The behavior of the diaphragm after phrenicoexairesis. *Am. J. M. Sc.*, 1934, *187*, 338–347.

Changes resultant from phrenicoexairesis were studied in 138 cases. In all of these, preliminary roentgenoscopy and roentgenography was performed to record the position and mobility of the diaphragm. Subsequent comparisons showed the following changes: (1) rise of the diaphragm into the thoracic cavity, (2) paradoxical motion and (3) ultimate fixation. In 8.7 per cent of the cases, however,

there were no changes in position. On the right side, the average rise was 4.3 cm.; on the left, 4.7 cm. No appreciable increase in effect was noted when exairesis was performed versus phrenicotomy. In many of the cases the maximum rise was noted within a period of six months, though in a few elevation continued after this time. In some cases there subsequently followed a descent to the extent of 2 or 3 cm. The change in position of the diaphragm seemed to be dependent upon: (1) the amount of suction force as produced by the negative intrathoracic pressure, (2) the upward push as effected by a positive intra-abdominal pressure. The author emphasizes that the first of these factors is influenced by the amount of parenchymal infiltration, fibrosis and pleural adhesions. Therefore, some of the most extreme cases showed the least benefit—because the amount of parenchymal and pleural involvement lessened the intrathoracic suction and at the same time because of the loss of tone of the abdominal muscles they had a subnormal intra-abdominal pressure. During the earlier periods, that is, from two to eighteen months after the operation, paradoxical movements of the diaphragm were the rule. Ultimately, however, probably because of degeneration and atrophy of the diaphragmatic musculature plus pleural adhesions, fixation occurred.—*A. A. de Lorimier.*

Fried, B. M. Bronchiogenic cancer combined with tuberculosis of the lungs. *Am. J. Cancer*, Feb., 1935, *23*, 247–266.

In some patients, multiplicity of pathological conditions must be considered. Formerly the idea was promulgated that one disease mitigates against the development of another. Even today, pathologists hesitate to diagnose multiple primary foci in cases of malignancy. Some conditions are especially not uncommonly seen together such as diabetes with tuberculosis or either of these conditions with malignancy.

Synopses of 13 case records are presented, in all of which both tuberculosis and carcinoma were found to involve the same lung. The tuberculous processes were in the healing fibrotic stage. Carcinomatous changes were conspicuously found where a fibrinous meshwork could be seen to be paving the way for epithelialization over formerly active lesions; these changes were never found in sites of caseation. Tubercle bacilli were recovered from the sputum in only 3 of the 13 cases. The author stresses the fact that carcinoma should be considered particularly in patients past middle age where the objective findings are out of proportion to such complaints as rapid loss of weight, weakness, pain in the chest and hemoptysis. In most of the cases, the definite diagnosis cannot be established until post-mortem studies; frequently roentgenography will be convincing; in some, biopsies can be performed by way of bronchoscopy or by excision of supraclavicular nodes. One of the cases reported presented the symptoms and signs of the so-called "superior sulcus tumor."—*A. A. de Lorimier.*

Hedblom, Carl A. Diaphragmatic hernia. *Ann. Int. Med.*, Aug., 1934, *8*, 156–176.

This is a very complete discussion on the subject. The author details considerations as to embryology, classification, incidence, frequency of location, etiology, symptoms, physical findings, diagnosis, roentgenographic manifestations, complications, indications for operation and treatment. His classification includes three types of diaphragmatic herniations: congenital, acquired and traumatic. He questions the inclusion of such conditions as "thoracic stomach" or the "hiatus hernia of Åkerlund." Depending upon the age of the patient and his position during examination this latter condition has been noted in anywhere from 8 to 73 per cent of patients. He quotes Harrington as having been able to insinuate at least one finger between the muscular ring and the esophagus in 35 per cent of abdominal examinations. Compiling various reports of definite herniations about 78 per cent of the nontraumatic and 95 per cent of the traumatic cases were found on the left side. Those located in the "foramen of Bochdaleki" were usually uncovered by peritoneum—signifying the failure of closure of the pleuroperitoneal membranes. Very few cases of failure in development of the diaphragm reached adult life. In 20 per cent of a series of 857 cases, the stomach alone was herniated; in 10.3 per cent, the colon alone; in 9.5 per cent, the omentum alone; rarely the liver or spleen alone; otherwise the herniations showed various combinations of abdominal viscera including even the pancreas and kidney.

Of the congenital herniations about one-third died before one month of age; about two-thirds of the traumatic variety occurred in the second, third or fourth decades, while the other-

wise acquired types were usually seen in the later years of life. Factors such as straining at stool, coughing, vomiting, labor, loss of fatty deposits between the serous membranes, etc., are believed to be etiological possibilities concerned with the latter types. For the traumatic variety, blunt or penetrating injuries such as falls, violent strains, gun shot or surgical wounds, etc., were the factors.

Both thoracic and abdominal symptomatology might be noted. Of the former might be mentioned: dyspnea, cyanosis, palpitation, dysphagia, substernal or shoulder pains, coughing and hiccough. Such symptoms are usually aggravated by the lying position or by eating or drinking. Abdominal symptoms include burning or colicky pains simulating peptic ulcer or even gallbladder diseases, perhaps nausea, vomiting, hemoptysis, melena and even evidence of definite obstruction. By physical examination of the thorax there might be noted displacement of the heart, abnormal areas of dullness and thoracic borborygmi. Positive diagnosis and differentiation of this condition from eventration usually rests with roentgenoscopic and roentgenographics tudies. For this the horizontal or Trendelenburg position should be used.

Complications to be considered include intestinal obstruction, acute respiratory failure, ulcerations, shock and hemorrhage. With prolonged evidence of obstruction, gangrene and rupture must be borne in mind. Except in those cases of small reducible herniations, surgery should be performed. Where obstruction has developed and the patient has been exhausted by persistent vomiting the mortality risk is increased about two and a half times. Preliminary operations include enterostomy, phrenic nerve crushing and perhaps thoracoplasty. The author's mortality risk has been about 14 per cent.—*A. A. de Lorimier.*

Leggett, Elizabeth A., Myers, J. Arthur, and Levine, Ida. Spontaneous pneumothorax. *Am. Rev. Tuberc.*, 1934, *29*, 348–361.

The foundation of our knowledge of pneumothorax rests on the studies of Itard (1803) and Laennec (1819). Pneumothoraces may be divided into two groups: (1) those resulting from trauma whether accidental or intentional, and (2) those resulting spontaneously from some pathological process in the individual.

Nearly all writers place tuberculosis at the head of the list of the pathological processes causing spontaneous pneumothorax. Acute pulmonary conditions such as pneumonia, empyema, lung abscess, pulmonary gangrene, bronchiectasis, emphysema, pulmonary infarct, and hydatid disease have been recognized as causes.

A higher percentage of idiopathic spontaneous pneumothoraces are seen in office and consultation practice than in hospital or sanatorium practice.

It is to be remembered that recurrent spontaneous pneumothoraces occur. Robertson and Watson have reported one case with 8 recurrences in five years. Locke has reported one with 18 recurrences in seven years. In the first case there was no roentgen evidence of pathology after lungs were expanded.—*L. H. Osmond.*

Lins, Aguinaldo. Diagnostico differencial dos aneurysmas da aorta. (Differential diagnosis of aneurysms of the aorta.) *Rev. brasil. de tuberc.*, Jan.–Feb., 1934, *3*, 303–311.

The differential diagnosis of aneurysms of the aorta is based on: (*a*) roentgen geometry; (*b*) topographical anatomy; (*c*) the statics of the thorax; (*d*) the shadows, and (*e*) the evolution of the shadows.

Under roentgen geometry the author discusses the importance of angles of incidence in bringing out contrast between the tissues. Under topographical anatomy he discusses the direction taken by aneurysms of the different parts of the aorta—the ascending and descending aorta and the arch; if there are dense and homogeneous shadows which cannot be detached from the aorta in any direction of incidence and the lungs are transparent along their line of contact with the mediastinum it argues for aneurysm.

Under the statics of the thorax he says that the distribution of intrathoracic forces depends on atmospheric pressure and the elasticity of the lung tissue. In infiltration of the lung there is retraction on the side of the infiltration but, on the contrary, when an aneurysm invades one side of the thorax the elastic retraction of the lung decreases and there is deviation of the mediastinum toward the opposite side.

The density of the shadow of aneurysm is that of solid tissue in general and does not serve for differential diagnosis; but sometimes there are calcifications in the walls which are an aid in diagnosis. The pictures of hepatization show the transparent bronchial tree. Juxta-mediastinal effusions have distinct outlines and

change in form with change of the patient's position. Pericardial effusion cannot be dissociated from the heart outline while the shadow of aneurysm can. Lung cysts have an extensive line of contact with lung tissue while aneurysms have a broad base of implantation on the mediastinum. Escudero says that the differential diagnosis of hydatid cysts depends on the visibility or invisibility of rib shadows, but the author says this depends on the depth of solid tissue or liquid and on roentgen technique.

The evolution of the shadows is also significant in differential diagnosis. Manoel de Abreu worked out curves for the development of the shadows in different conditions. In pneumonia the curve is discontinuous and not uniform; progress is very rapid and retrogression also very rapid. In tuberculosis of the hyperacute form the curve is continuous, uniform and extremely rapid. In the acute and chronic progressive and regressive forms the curves are discontinuous and not uniform. In cancer the curve is continuous and shows uniformly accelerated velocity and rapid progress. In aneurysm of the aorta the curve is continuous and uniform and the progress slow. The outline of the mass extends centrifugally from the mediastinum to the lateral walls of the thorax, its long axis following more or less the bisector of the angle formed by the direction of the systolic impulse and the center of gravity.—*Audrey G. Morgan.*

Dillon, J. G., and Gurewitsch, J. B. Herzmessungen in dorsoventralen und schrägen Durchmessern und ihre klinische Bedeutung. (Measurements of the heart in the dorsoventral and oblique projections and their clinical importance.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1935, *51*, 180.

The authors discuss the various methods of cardiac measurement and as the result of their experience in 90 cases examined by the Fray technique they conclude that this is the best method for determining the size of the ventricles.—*E. T. Leddy.*

Weltz, G. A. Die pulsatorischen Bewegungen der Brustaorta. (The pulsatory movements of the thoracic aorta.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1935, *51*, 152.

By means of surface kymography and densography it is possible to demonstrate marked differences in the movement in the right and left side of the aorta. Weltz here illustrates and analyzes these differences and points out their significance and importance in the diagnosis of aortic disease.—*E. T. Leddy.*

Kahlstorf, Adolf, and Ohnesorge, E. Die diagnostische Bedeutung der pulsatorischen Aortenbewegungen im Flächenkymogramm. (The diagnostic importance of the pulsatory movements of the aorta as determined by the surface kymogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1935, *51*, 22.

The authors studied the movements of the normal and pathologic aorta with the surface kymogram and found the following deviations from the normal "hook-shaped" lateral movement: in aortic insufficiency the indentations are long and pointed, in the whole ascending aorta, the so-called sling motion. In luetic mesaortitis there is marked lateral movement in the nonthrombosed portions which are the diseased parts of the media. In aortic aneurysm there may be complete absence of pulsation in extensive thrombosis of the marginal sections so that a mediastinal tumor cannot in some cases be excluded by the kymogram alone. In sclerosis and hypertension the movements of the ascending aorta in general are somewhat less than normal, and the movements of the whole aorta more uniform and the lateral movements more oblique. But there are no kymographic characteristics which differentiate sclerosis from hypertension. All changes in the shape and extent of the movements as well as their irregularities are most marked in the ascending aorta and are generally absent in the descending aorta.—*E. T. Leddy.*

Sigler, Louis H., and Schneider, J. Jacob. The diagnosis of cardiac aneurysm with report of two cases. *Ann. Int. Med.*, March, 1935, *8*, 1033–1046.

Detailed reports of 2 cases and a brief additional summary of a third case of cardiac aneurysm are presented. All of these cases showed evidence of coronary occlusion, though one of the patients was only thirty-three years of age. The authors stress the fact that coronary disease is the most frequent precursor of these aneurysms. Very rarely there is the background of a congenital defect, or of an endocarditis, or even of trauma.

Subjective symptoms are not specific; simply those of cardiac failure presenting the anginal syndrome. Actual aneurysm is rela-

tively rare. Lucke and Rea found the heart so involved in only 1.25 per 1,000 autopsies—or in 4.64 per cent of the total number of aneurysms. Hall's series showed that 74 per cent of the cases occurred in males. Most of the recorded cases have not been recognized until post-mortem examination. The authors consider clinical evidence to be of greater value than either the electrocardiographic or roentgenographic. The following criteria are most important: (1) prominence and diffuse heaving character of the apical impulse, (2) extreme weakness of the first sound over that area, (3) presystolic gallop rhythm, (4) localized systo ic murmur and (5) a weak pulse (because of a low systolic and relatively high diastolic pressure). Libman has emphasized the finding of "a pulsation more marked between the apex and sternum than at the apex." Roentgenography should include the several oblique projections and should be substantiated with roentgenoscopy. Secondary calcifications might be visualized.—*A. A. de Lorimier.*

ABDOMEN

Pinke, J. Über den Wert der Röntgenuntersuchung bei ungewöhnlichen Krankheitsformen des Verdauungskanals. (The value of roentgenologic examination in some of the more unusual forms of gastrointestinal disease.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1935, *51*, 261.

Pinke reports 5 rare conditions in the gastrointestinal tract: (1) temporary blocking of the duodenal bulb by a gastric polyp, (2) an encysted gas bubble in the space between the stomach and liver caused by an ulcer, (3) a gastrocolic fistula with no clinical signs, (4) diverticulosis of the duodenum and small intestine, with gastroenteritis, and (5) a diverticulomyoma of the duodenum.—*E. T. Leddy.*

Lotzin, R. Über das Faltensystem des Magens und seine Beziehungen zum Gefässsystem. (The rugae of the stomach and their relationship to the vascular system.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1935, *51*, 329.

The author shows that the variations in the mucosal folds of the adult stomach from the scheme of longitudinal folds of Chaoul are an effect of the submucosal vascular system beneath them. The development of the rugae in the fetus and their gradual changes due to the development of the vascular network are described. The author concludes from his study that the variations of the mucosal folds from the longitudinal fold scheme are due to special anatomical factors and that the motility of the mucous membrane has no effect on the configuration of the rugae.—*E. T. Leddy.*

Forssell, G. Ein Beitrag zur Kenntnis der Verteilung der Arterien der Submukosa und der Mukosa des Magens im Verhältnis zum Schelimhautrelief. (A contribution to the knowledge of the distribution of the arteries in the submucosa and mucosa of the stomach in relation to the mucosal relief.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1935, *51*, 338.

The arrangement of the folds of the gastric mucosa is not determined by the arteries in the submucosa but on the other hand the arterial branches move with or are displaced by the movements of the rugae. There is no difference between the longitudinal and transverse folds in regard to the distribution of the submucosal vessels in the rugae.—*E. T. Leddy.*